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Midwest Research Inst, Kansas City, Mo

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SUBSTITUTE CHEMICAL PROGRAM

INITIAL SCIENTIFIC AND MINIECONOMIC REVIEW OF CARBOFURAN

JULY 1976

U.S. ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PESTICIDE PROGRAMS
CRITERIA AND EVALUATION DIVISION
WASHINGTON, D.C. 20460

EPA 540/1-76-009

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PREFACE

The Alternative (Substitute) Chemicals Program was initiated under Public Law 93-135 of October 24, 1973, to "provide research on, and testing of, substitute chemicals." The legislative intent is to avoid the use of substitute chemicals that would be even more deleterious to man and his environment than a pesticide that is cancelled or suspended for causing "unreasonable adverse effects to man or his environment." The major objective of the program is to determine whether potential substitute chemicals are suitable replacements for cancelled or suspended pesticides or for pesticides that are under litigation or are candidates for Rebuttable Presumption Against Registration (RPAR).

The review of the substitute chemical considers its chemistry, toxicology, and pharmacology as well as its use patterns, efficacy, and environmental fate and movement. EPA realizes that, even though a compound is registered, it still may not be a practical substitute for certain uses of a problem pesticide. Therefore, the utilitarian value of the "substitute" must be established by reviewing its biological and economic data.

The reviews of substitute chemicals are carried out in two phases. Phase I Initial Scientific Review evaluates the "safety and efficacy" of the substitute chemical based on data readily accessible at the present time. The Phase II Integrated Use Analysis examines the effects of possible regulatory action against a hazardous pesticide for each of its major and critical uses. The examination considers the suitable substitutes in conjunction with alternative agricultural management practices. Current and projected environmental, health, and economic impacts are also evaluated.

This report contains the Phase I Initial Scientific Review of carbofuran. Carbofuran was identified as a registered substitute chemical for certain problematic uses of chlordane, heptachlor and aldrin which have been cancelled by EPA. The report covers all uses of carbofuran and is intended to be adaptable to future needs. Should carbofuran be identified as a substitute for a problem pesticide other than those mentioned above, the review can be updated and made readily available for use. The data searches ended in June, 1975. The report summarizes rather than interprets scientific data reviewed during the course of the studies. Data from different sources is not correlated, nor are opinions presented on contradictory findings.

A team of EPA scientists in the Criteria and Evaluation Division of the Office of Pesticide Programs coordinated the review; the team leader provided guidance and direction and technically reviewed information retrieved during the course of the study. The following EPA scientists comprised the review team: E. Neil Pelletier, Ph.D. (Team Leader); Padma Datta, Ph.D., and Hudson Boyd (Chemistry); Roger Gardner (Pharmacology and Toxicology); Willard Cummings and Richard Stevens (Fate and Significance in the Environment); Ralph Wright (Registered Uses); and Gary Ballard and Harry Gaede, Ph.D. (Economics).

Data research, abstracting, and collection were performed primarily by Midwest Research Institute (MRI), Kansas City, Missouri (EPA Contract #68-01-2448) under the direction of Thomas L. Ferguson. The following MRI scientists were principal contributors to the report: Alfred F. Meiners, Ph.D.; James V. Dilley, Ph.D.; Frank E. Wells, Ph.D.; William J. Spangler, Ph.D.; David F. Hahlen; and Thomas L. Ferguson. Other MRI project team members who contributed to the development of this review were John R. Hodgson, Ph.D.; Edward W. Lawless, Ph.D.; Daniel G. Puzak, and Kathryn Lawrence. Rosmarie von Rumker, Ph.D., and Freda Horay, both of RvR Consultants, were also contributors.

The scientific staffs of EPA's Environmental Research Laboratories reviewed draft copies of the report. Comments and supplemental material provided by the following laboratories were greatly appreciated and have been incorporated into this report: Gulf Breeze Environmental Research Laboratory, Gulf Breeze, Florida, and the National Ecological Research Laboratory, Corvallis, Oregon. FMC Corporation, which manufactures carbofuran, and the Chemagro Division of Mobay Chemical Corporation, which markets carbofuran under a license from FMC, both reviewed the draft of this report and made certain comments and additions.

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PART I. SUMMARY

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This section contains a summary of the "Initial Scientific and Minieconomic Review" conducted on carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate). The section summarizes rather than interprets data reviewed.

Production and Use

Carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate) is a broad-spectrum insecticide-nematicide, especially effective against corn rootworms. Carbofuran is manufactured by FMC Corporation (owner of the manufacturing and use patents) at Middleport, New York, and is also marketed under license by the Chemagro Division of Mobay Chemical Corporation.

Carbofuran is a white crystalline solid that undergoes alkaline hydrolysis (cleavage at the carbamate linkage), oxidation and photodecomposition. Carbofuran is readily metabolized by plants, animals, insects, and soil microorganisms. Oxidation and photodecomposition appear to be minor environmental degradation routes. (See Figure 1.)

Carbofuran is available in 4 granular formulations (2, 3, 5, and 10%) and a 4 lb/gal flowable formulation. The only formulations available for domestic use are those made by the manufacturer; carbofuran is not available in the United States as a technical active ingredient.

Carbofuran production in 1972 was estimated at 6 million lb active ingredient (AI), approximately 1 million lb of which were exported. Estimated 1974 domestic usage was slightly over 7.0 million lb. Approximately 6.8 of the 7.0 million pounds were used on corn (6.3 million lb in the corn belt, lake and northern plains states; 500,000 lb in the remaining corn-growing states).

Toxicity and Physiological Effects

Acute Toxicity - In tests with various animal species, chickens appeared to possess the greatest resistance to carbofuran (LD_{50} = 25.0 to 38.9 mg/kg) and mice, the least resistance (LD_{50} = 2 mg/kg). Dogs were intermediate (LD_{50} = 18.85 mg/kg). Sex differences were not apparent.

In tests with rats the acute toxicity of carbofuran was found to be as follows:

Route of administration	Formulation	Measurement	Value
Oral	Technical (98.8%)	LD_{50}	1.65 mg/kg (newborn) 3.36 mg/kg (weanling) 6.4 to 14.1 mg/kg (adult)
Intraperitoneal	Technical (98.8%)	LD_{50}	1.37 mg/kg

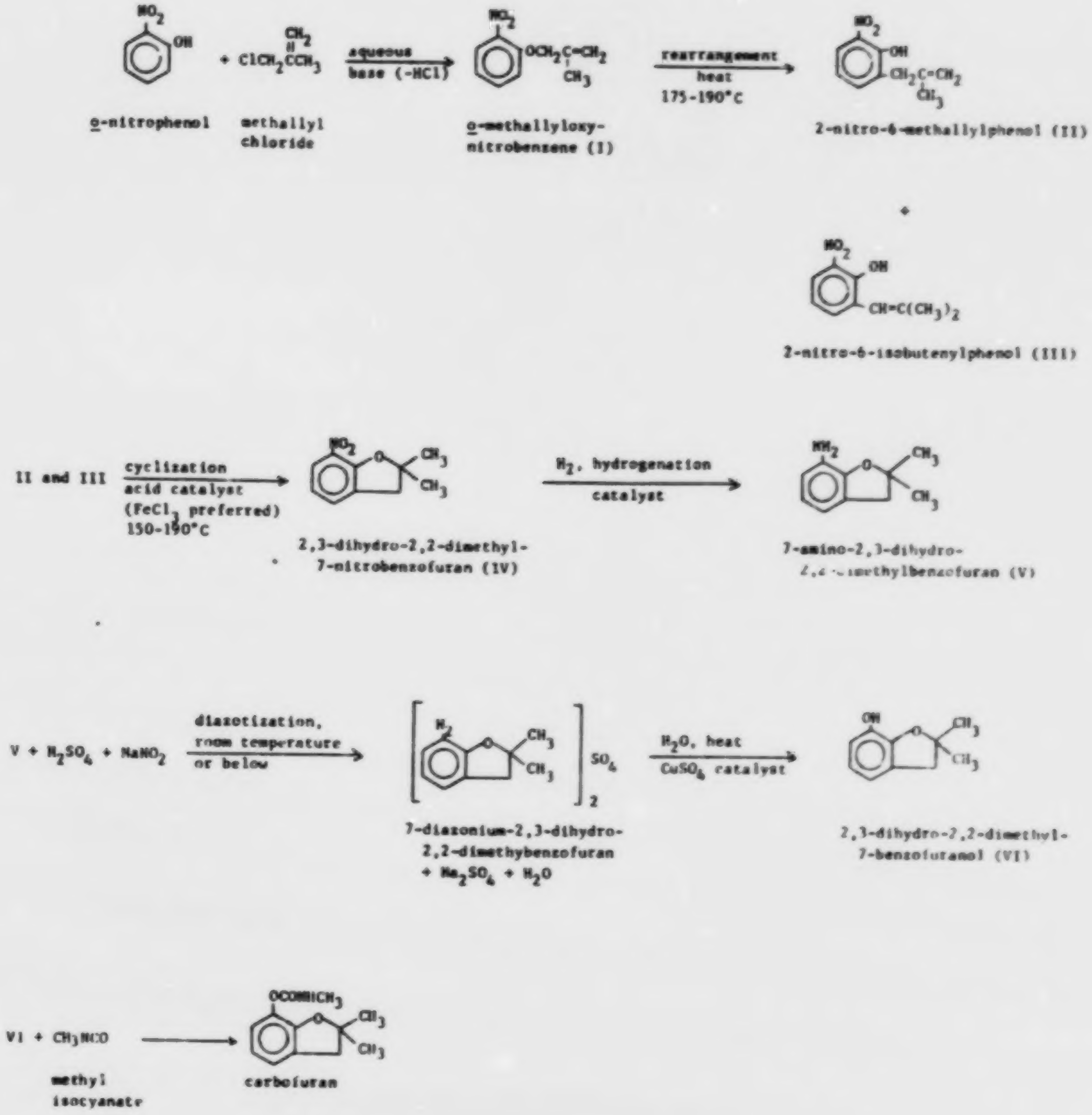
o-nitrophenol
+ ClCH2CCH3 (=CH2)
methallyl chloride
aqueous base (-HCl)
o-methallyloxy-nitrobenzene (I)
rearrangement heat 175-190°C
2-nitro-6-methallylphenol (II)
+
2-nitro-6-isobutenylphenol (III)
II and III
cyclization acid catalyst (FeCl3 preferred) 150-190°C
2,3-dihydro-2,2-dimethyl-7-nitrobenzofuran (IV)
H2, hydrogenation catalyst
7-amino-2,3-dihydro-2,2-dimethylbenzofuran (V)
V + H2SO4 + NaNO2
diazotization, room temperature or below
7-diazonium-2,3-dihydro-2,2-dimethybenzofuran + Na2SO4 + H2O
H2O, heat CuSO4 catalyst
2,3-dihydro-2,2-dimethyl-7-benzofuranol (VI)
VI + CH3NCO
methyl isocyanate
carbofuran

Figure 1. Manufacturing Process for Carbofuran

The acute dermal LD_{50} for rabbits of technical carbofuran in an organic solvent (Dowanol DPM) was 14.7 mg/kg; however, the acute dermal LD_{50} of the technical carbofuran in water was greater than 10.2 g/kg. A 10% granular formulation (10G) had an LD_{50} of 10.2 g/kg. Furadan® 4 flowable had a dermal LD_{50} value of 6.8 g/kg.

In studies on the effects of carbofuran metabolites on rats, 3-hydroxycarbofuran was found to be highly toxic; 2,3-dihydro-7-hydroxy-2,2-dimethyl-3-oxobenzofuran and 3-ketocarbofuran moderately toxic; and 2,3-dihydro-2,2-dimethyl-7-hydroxybenzofuran and 2,2-dimethyl-3,7-dihydroxy-2,3-dihydrobenzofuran, slightly toxic.

In tests with 1- to 2-week-old calves, a single dose of carbofuran at 1 mg/kg resulted in death; the same dose in older animals resulted only in salivation, tearing, hyperactivity and diarrhea.

Sheep exhibited increased salivation, stomach cramps, and frequent micturition at carbofuran doses higher than 2.5 mg/kg. At 10 mg/kg dosing, death occurred, even though the animals were treated with atropine sulfate.

Subacute Toxicity - The subacute effects of carbofuran were evaluated in tests using rats, rabbits, guinea pigs, chickens, and dairy cows.

Rats fed 0.1 to 1,600 ppm carbofuran for 90 days did not exhibit abnormal changes when compared to controls; comparisons were made of gross pathology, histopathology, hematology, and urine constituents. Although no deaths were recorded, animals that received diets containing carbofuran at 1,600 ppm exhibited slight to moderate, generalized tremors.

Other rats were fed at dietary levels up to 3,000 ppm for 90 days without significant observable differences between test groups and controls. Comparisons were made of hematology, urine constituents, blood chemistry, gross pathology, and histopathology.

As part of a 16-week study, rats were dosed after 13 weeks with carbofuran at levels of 0, 0.1, 0.3, 1.0, and 3.0 mg/kg/day. A slight reduction in cholinesterase values at the highest dose occurred.

A study in which female rats were given 3 mg/kg/day for 3 weeks showed that the time of testing for cholinesterase activity after dosing is important. Samples taken from 0 to 60 min after administration of carbofuran showed greatest cholinesterase inhibition a short time after treatment.

At 5 mg/kg/day, cholinesterase activity in dogs treated for 92 days was not radically reduced (the dogs exhibited frequent coughing and gagging). Daily exposure to carbofuran resulted in some adaptation to the pesticide. The depression of cholinesterase activity after a single dose given to rats previously exposed to carbofuran for 14 to 28 days was not as great as that which occurred in rats that had not been previously exposed.

Rabbits fed a diet containing 700 ppm carbofuran for 14 days showed a slight decrease in body weight. No other effects were noted.

Three metabolites of carbofuran (3-hydroxycarbofuran phenol, 3-ketocarbofuran phenol, and carbofuran phenol) were fed to chickens for 28 days without any apparent adverse changes in appearance, behavior, food consumption, or egg production. These same metabolites were also fed to dairy cows in combinations up to 200 ppm (66.7 ppm dietary for each metabolite) for 28 days. No abnormal effects were observed in any test animal.

Chronic Toxicity - Two-yr chronic studies were conducted with rats and dogs. Rats were given carbofuran at dietary levels of 1, 10, and 100 ppm. Both males and females in the 100 ppm test group exhibited a weight depression, but the lowered rate of gain was statistically significant in males only ($P < 0.05$). In all other measurements, no differences were observed between the untreated controls and treated animals. Comparisons were made by hematological tests, tests for urinary constituents, blood chemistry tests, and gross pathology and histopathology.

An additional study was performed at dietary levels of 25 and 50 ppm. The only differences noted between treated and control rats was a reduction in food consumption by males at the 50 ppm level for the first 9 months of the test. All other comparisons (mortality, behavioral reactions, gross pathology, and histopathology) did not demonstrate any differences between the untreated controls and the animals fed the 50-ppm diet.

In a 2-yr chronic study with dogs, no abnormal behavioral reactions were observed in animals fed 1, 2, 10, 20, and 50 ppm carbofuran diets. At 100 ppm, slight coughing and gagging reactions were observed. At 200 and 400 ppm, coughing and gagging were observed daily. Muscular tremors and weakness in the hinquarters were also seen in dogs fed 200 ppm. Death occurred in some animals at 400 ppm.

Effects on Reproduction - A 3-generation reproduction study with rats fed a 1, 10, and 100 ppm showed a low 5-day survival index for pups and a greater incidence of stillbirths in the 100 ppm test group. In another test conducted at 50 ppm, results for F_0 parents and F_{1a} and F_{1b} progeny paralleled the 100 ppm study. The 5-day survival indexes for the progeny from the treated animals were lower than those of the controls; weanling body weights were also lower in treated than in untreated animals.

A 3-generation study at 20 and 30 ppm carbofuran suggested that the 30 ppm treatment level (a) affected the mating of parental animals, and (b) had an effect on the 5-day survival index of progeny from treated parents.

Three metabolites of carbofuran fed to rats at 10 and 50 ppm apparently did not have any effect on the ability of the animals to mate, conceive, or to carry their young.

A reproduction study with dogs indicated that dietary levels of carbofuran at 20 and 50 ppm for 20 months had no adverse effects on parental animals with respect to mortality, estrus cycles, mating, parturition or lactation. Treatment of parents did not affect progeny with respect to litter size, survival indices, or ability to nurse. When pregnant bitches were fed carbofuran at 20 ppm during the last half of gestation, no effects were observed in the pups or the mother. All pups appeared normal and maintained normal growth patterns.

Carcinogenicity - The incidence of tumors in rats fed dietary levels of 10 ppm carbofuran for 2 yr was no different than in untreated controls. Similar results were observed in a study at 50 ppm.

Mice were fed carbofuran at 30 and 100 ppm for 18 months in a study to determine whether or not carbofuran was carcinogenic by oral routes. The percent of mice bearing tumors at the end of the study (10.5%) was the same for the controls and for the animals treated at 100 ppm. In a positive control group (treated with urethane) 76% of the animals had tumors.

Mutagenesis - One study with mice indicated that a dose of 0.5 mg/kg carbofuran did not induce a dominant lethal mutation in mice.

Teratology - Female rabbits were administered carbofuran in gelatin capsules (0.1 and 0.5 mg/kg/day) beginning on the sixth day of gestation and continuing through the eighteenth day. On the twenty-ninth day of gestation the does were sacrificed and the litters recovered by caesarian section. Examination of 120 fetuses failed to reveal any abnormalities that could be attributed to exposure to carbofuran. It appeared, however, that resorption was twice as high in the carbofuran test groups as in the controls.

Potentiation - Twelve pesticides were included in a study to determine whether or not combination with carbofuran resulted in potentiation. No potentiation as determined by acute oral toxicity was observed.

Signs and Symptoms - Depending on dose, signs and symptoms reported for carbofuran intoxication were similar in most animals. These included fibrillary action, salivation, ataxia, exophthalmos, hyperpnea, tonoclonic convulsions, labored breathing, affected limbs (weakness, paralysis), depression, prostration, and death.

Antidotes - Studies with rats, dogs, rabbits, cattle, and sheep indicated that treatment of affected animals with atropine sulfate could reverse the toxic effects of carbofuran if treatment was started early enough. A 50 mg/kg dose was effective in rats and dogs. A 10 mg dose of atropine sulfate protected rabbits from lethal effects of carbofuran at 5.3 mg/kg. The results of one study with rats, however, indicated that 2-pyridine aldoxime methochloride (2-PAM) was not antidotal.

Eye Irritation - Instillation of 5 mg of technical carbofuran into the conjunctival sac of the eyes of New Zealand white rabbits resulted in miosis for a period of 2 hr. Thereafter, the condition cleared.

Skin Irritation - Intracutaneous injection of technical carbofuran into the skin of male guinea pigs every other day for 20 days (0.05 ml initial injection and all others 0.10 ml) did not elicit a sensitizing reaction.

Neurotoxicity - White leghorn hens dosed with technical carbofuran at concentration equivalent to the reported LD_{50} (38.9 mg/kg) exhibited salivation and general weakness, but not leg and wing weakness. Surviving birds were given a second dose at day 21 with similar results. No physical signs of neurotoxicity were observed.

Metabolism - The main pathway of oxidative metabolism of carbofuran in animals (and in plants and insects) appears to consist of hydroxylation at the benzylic carbon to yield 3-hydroxycarbofuran (2,3-dihydro-2,2-dimethyl-3-hydroxybenzofuranyl-7-methylcarbamate). The hydroxylated product is further oxidized to give 3-ketocarbofuran (2,3-dihydro-2,2-dimethyl-3-ketobenzofuranyl-7-N-methylcarbamate). Hydrolysis and conjugation then result. Carbofuran can also be hydrolyzed to carbofuran phenol (2,3-dihydro-2,2-dimethyl-7-hydroxybenzofuran). In addition, hydrolysis can occur following oxidation to 3-hydroxycarbofuran (or 3-ketocarbofuran). The 3-keto compound is hydrolyzed at a much faster rate than carbofuran.

The available data also indicates that hydrolysis is generally preceded by oxidative metabolism. The hydroxylated metabolites can be conjugated as glucosides in plants, or glucuronides in animals. Carbofuran metabolites are stored in plants but are not reported to accumulate or persist in animal tissues or milk.

Food Tolerances and Acceptable Intake

Carbofuran has not been reported as a significant residue in any class of food, nor is it detected by the Food and Drug Administration analytical system routinely used to monitor pesticide residues in food.

Tolerances have been established for "carbofuran" (evaluated as carbofuran plus its 4 major metabolites, and total carbamates) for 24 food and feed commodities. These tolerances range from 0.05 ppm (including a maximum 0.02 ppm carbamates) in meat, fat, and meat by-products to 40 ppm (including a maximum 20 ppm carbamate) in alfalfa hay. See page 37

An acceptable daily intake (ADI) has not yet been proposed for carbofuran.

Environmental Effects

Fish - Ten species of fish were used in laboratory testing of the toxicity of carbofuran. From all tests, the 96 hr LC_{50} ranged from 0.08 to 1.18 ppm. The toxicity of carbofuran varied considerably depending upon the species of fish and the physical conditions associated with the tests. For example, the LC_{50} (24 hr) of carbofuran to brown trout was 0.355 mg/l (ppm) in city water, but was found to be 0.842 ppm in reconstituted standard water.

The bluegill appeared to be the most sensitive species and the fathead minnow the most resistant. Intoxicated fish were at first hyperactive, but this stage was followed by lethargy, body paralysis, scoliosis, loss of equilibrium, opercular paralysis, and death.

When 3% granular carbofuran was applied to rice fields at the rate of 0.5 lb AI/acre, some casualties fo mosquitofish (Gambusia affinis) occurred 1 hr after treatment. Heavy mortality of mosquitofish, large-scale menhaden (Brevoortia patronus), Atlantic croaker (Micropogon undulatus) and European carp (Cyprinus carpio) was found 24 and 48 hr after treatment. The rice seed used to plant the fields had been treated with another insecticide. If, and to what extent, the seed treatment may have influenced the fish mortalities is unknown.

Lower Aquatic Animals - Carbofuran was of intermediate toxicity (compared to several other commonly-used insecticides) to lower aquatic animals in one test, highly toxic in another test. The LC_{50} for white river-crawfish and bullfrog tadpoles was 500 and 2,700 ppb, respectively. The LC_{50} for Daphnia magna was 20 ppb. The 24- and 48-hr ED_{50} values for pink shrimp exposed to technical carbofuran were 0.0068 and 0.0046 ppm, respectively. Technical carbofuran did not appear to affect the eastern oyster in exposures up to 96 hr at 1.0 ppm.

In a field study, carbofuran granules (0.5 lb AI/acre) resulted in heavy mortality of cricket frogs, crayfish, earthworms, and nontarget aquatic insects between 1 and 45 hr after treatment.

Wildlife - Data on carbofuran's toxicity to wildlife demonstrates that the oral LD_{50} to 8 species of adult birds for technical grade carbofuran ranged from 0.238 mg/kg for the fulvous tree duck (Dendrocygna bicolor) to 8.0 mg/kg for the bobwhite quail (Colinus virginianus). Dermal toxicity was 100 mg/kg in tests with 2 species (house sparrow, Passer domesticus, and quelea, Quelea quelea.

Oral LD_{50} for Furadan 10G ranged from 0.71 mg/kg for mallard ducks (Anas platyrhynchos) to 100 mg/kg for bobwhite quail.

Subacute toxicity studies indicated that the mallard duck was the most sensitive of the birds studied (oral LD_{50} = 0.397 mg/kg) and that the bobwhite quail was the most resistant (oral LD_{50} = 8.0 mg/kg) to technical grade carbofuran. Toxicity symptoms among the surviving bird species lasted from 5 to 7 days and occurred as soon as 5 min after treatment.

Carbofuran fed to quail for 6 weeks was not highly toxic at levels of 200 ppm or less, but was highly toxic at 400 ppm. Feed efficiency decreased at dietary levels above 200 ppm.

Although sex differences were not observed with single acute doses, the males appeared to be more susceptible than females to extended, subacute dosing.

The fertility of females and the hatchability of eggs were greatly reduced at levels of 200 ppm and above. However, no abnormal embryos or hatchlings were observed.

In one field study on the effects of carbofuran on wildlife, an application of 3% granular carbofuran to rice fields at a rate of 0.5 lb AI/acre resulted in bird death or illness at 17 and 24 hr after treatment, with anywhere from 1 to 8 carbofuran granules in their stomachs. In 5 other field studies, no mortality or significant adverse effects on mallard ducks, bobwhite quail, and ring-neck pheasant resulted from exposure to various carbofuran formulations.

Beneficial Insects - Carbofuran was highly toxic to honeybees (*Apis mellifera*) by direct contact. The LD_{50} was 0.16 μg/bee. No label warnings occur on granular carbofuran formulations since granulars apparently offer little or no hazard to bees.

Lower Terrestrial Flora - When applied at rates of 1 and 5 μg/g soil, carbofuran did not drastically reduce the fungal population. However, the higher rate did depress fungal populations at 1, 2, and 4 weeks, but at 8 and 12 weeks there was no significant difference between carbofuran-treated plots and untreated controls.

Carbofuran applied at 5 μg/g soil significantly decreased bacterial populations during the first week. However, bacterial populations soon recovered to previous levels or levels above controls.

The above studies also showed that carbofuran had no effect on ammonification or nitrification of ammonium from soil organic nitrogen. However, oxidation of elemental sulfur was significantly depressed.

Measurement of soil microbial respiration showed that oxygen consumption increased as carbofuran concentration increased. The authors concluded that soil microorganisms are able to tolerate carbofuran.

Carbofuran applied at 100 ppm and 10 ppm AI had little effect on soil respiration. Oxygen uptake in carbofuran-treated soil was slightly higher than the untreated control. Possible degradation of the formulation was indicated.

Other studies showed that carbofuran had no effect on nitrification at application rates of 5, 50, and 500 ppm. In addition, growth of the rhizobia bacteria Rhizobium meliloti and Rhizobium japonicum was not affected. However, there was some growth inhibition of Rhizobium leguminosarum and Rhizobium trifolii.

Legume seedling growth was studied at the 5, 50, and 500 ppm application rates using sweet clover and alfalfa. At the field application rate (5 ppm), carbofuran did not affect seedling growth. However, at 500 ppm, growth was drastically reduced.

The effects of carbofuran on microflora under field conditions were studied using field plots designed to approximate actual pesticide application and timing in the growing of shade leaf tobacco. Carbofuran depressed relative numbers of fungi, bacteria, actinomycetes, and algae, although not at a statistically significant level. Nitrification depression was also not statistically significant.

Carbofuran had no harmful effect on the Rhizobium species peanut (Arachis hypogaea) symbiosis when applied at normal field rates.

A study to determine the influence of carbofuran on the growth rate of 2 soil-borne fungi was conducted in vitro. The growth of Fusarium oxysporium f. lycopersici was slightly inhibited when grown on nutrient media containing 5 ppm carbofuran. The dry weight of Penicillium digitatum increased slightly.

The effects of 1,000 ppm AI carbofuran on microbial populations was studied. Twenty-four hr after application the average number of bacteria and fungi per gram of soil did not differ significantly between the treated and untreated samples.

When carbofuran (0.47g AI/100 ml) was added to commercial formulations of Bacillus thuringiensis, the survival of the bacteria on inert surfaces was not affected.

Lower Terrestrial Fauna - The effect of 10% granular carbofuran applications on earthworms (Lumbricus terrestris) was studied. Surface level dead and dying earthworm counts were made 6 days after application. Earthworms in the immediate area of 2.0 and 4.0 lb AI/acre carbofuran banded applications were killed in large numbers. The LD_{50} for earthworms was 1.3 mg/kg. When carbofuran was mixed with soil, the LC_{50} over a 5-day test period was 12.2 ppm. Studies using ^{14}C-labeled carbofuran indicated that earthworms metabolize carbofuran initially in a manner similar to other animals and plants. However, the study suggested that toxicity to worms was caused by factors other than cholinesterase inhibition.

The reactions of the manure worm (Eisenia foetida) were compared to those of earthworms (Lumbricus terrestris). Carbofuran appeared to repel E. foetida while seeming to immobilize L. terrestris. Carbofuran uptake in a 6-hr period was similar for both species. However, excretion of this material in 48 hr was 95% and 10%, respectively.

Bioaccumulation and Biomagnification - Bioaccumulation and biomagnification studies were performed using a terrestrial-aquatic model ecosystem with a 7-element food chain. The terrestrial phase of the system was treated with ^{14}C-labeled carbofuran at a rate equivalent to 1 lb AI/acre and allowed to run 33 days. At the end of the experiment, none of the organisms contained carbofuran, although several carbofuran metabolites were isolated from a freshwater plant, Elodea canadensis (maximum concentration 0.035 ppm).

Carbofuran was highly biodegradable, with low residual activity in the ecosystem. Detoxification occurred by hydroxylation of the carbofuran molecules. The authors concluded that carbofuran does not present ecological problems related to food chain accumulation or biomagnification.

Fate in Soil - The fate of carbofuran in soil was studied by incorporating 10% granules applied at 1.85 ppm (recommended rate) into soils. Soil concentration of carbofuran after 8 weeks was 20% of the original. Biological activity in sandy loam soil disappeared within 16 weeks. In muck soils, biological activity persisted for 24 weeks.

Degradation in soils of pH 7.8 was rapid; a tenfold difference in half-life was noted between soils of pH 4.3 and 7.8. Rapid chemical hydrolysis is the primary route of carbofuran degradation in alkaline soils. In acid and neutral soils, both chemical and microbial degradation mechanisms predominate, but overall degradation rates are slower.

Field investigations showed that carbofuran reached maximum insecticidal toxicity 3 to 5 days after application. Toxicity degradation in the 2 soils tested (pH 5.2 and 6.4) was approximately equal.

Time periods required for carbofuran toxicity to reach soil surfaces when incorporated into the soil at depths of 1/2, 3/4 and 1 in were 1, 2 to 3, and 3 to 4 weeks, respectively.

Three soil types were treated with 2.0 and 9.0 ppm ^{14}C-labeled carbofuran. Dissipation was more rapid in sandy loam soil than in muck soil with half-life ranging from 20 to 40 days.

Studies of carbofuran dissipation showed no correlation between climate and dissipation rate. However, dissipation was greater after broadcast application than after band or in-furrow application. In addition, studies showed no indication of soil residue increase with carbofuran applications in successive years.

Fate in Water - Little data was available on the fate or effects of carbofuran in water. Maximum carbofuran residues in water from rice fields treated with 0.5 lb AI/acre were as follows: 0.7 ppm 8 hr after a postflood application and 0.05 to 0.1 ppm 7 days after a preflood application.

Fate in Air and Nontarget Plants - Limited data was found on the fate or the effects of carbofuran residues in the air, or on effects of residues in nontarget plants.

Transport - In a test simulating application of carbofuran granules to flooded rice fields, carbofuran residues in quantities toxic to leafhoppers (test animal) moved laterally 22.5 cm in 48 hr.

Transport studies showed that carbofuran leaches more slowly in soils which are high in clay or organic matter. If soils are of the same clay content, movement is further in soils with lower exchange capacities.

In a lysimeter study, carbofuran residues after 1 yr were negligible in the top 1.5 ft of 2 heavy soils (high organic matter) but were distributed equally throughout the top 3 ft of the sandy loam soil. Field studies showed that carbofuran residues generally remain in the upper 6 in of treated soils. Below 6 in depths, concentrations were less than 0.1 to 0.2 ppm in most instances.

Runoff studies showed that major losses of carbofuran occurred only with early rainfall events. In an extensive 2-yr study, carbofuran losses represented only 0.5 to 2.0% of the total applied. Most of the carbofuran which was lost was found in the water, not the sediment.

Efficacy and Cost Effectiveness

Carbofuran is recommended for control of armyworms, corn borers, corn rootworms, wireworms, nematodes, flea beetles, thrips, leaf hoppers, aphids, Colorado potato beetles, rice water weevils, tobacco budworms, hornworms, mosquito larvae, potato tuberworms, and lygus bugs on crops, and several pests attacking trees. Crops which are affected by these pests include alfalfa, bananas, field corn, peanuts, peppers, potatoes, rice, sugarcane, and tobacco.

The efficacy and cost effectiveness of carbofuran in pest control are summarized below.

Alfalfa - The alfalfa weevil was controlled for 28 days when 0.5 lb/acre of carbofuran was applied to the crop. Carbofuran at 1.0 lb/acre gave effective control of the Egyptian alfalfa weevil when applied 80 days prior to cutting. Control of lygus bugs was achieved for up to 33 days, but control of aphids was effective for a shorter period and additional applications were needed.

Corn - Control of corn rootworms, the European and southwestern corn borers, and the armyworms in field corn was obtained at rates of 1.0 lb of carbofuran per acre or less, except for the Illinois region where rates of 2.0 to 3.0 lb/acre were needed to control corn borers. Yields were generally increased with improved control.

In the tests reviewed, control of nematodes in carbofuran-treated field corn was slightly better than in untreated checks, but yields were significantly increased. Control of wireworms in the tests reported was poor.

The use of carbofuran on field corn resulted in yield changes ranging from a loss of 6.6 bu/acre to a gain of 49.4 bu/acre, as compared to untreated test plots. Economic benefits from these yield changes ranged from a loss of $35.40/acre to a gain of $90.20/acre from the use of carbofuran.

Peanuts - Carbofuran is effective as a nematicide for control of root-knot, sting, and stunt nematodes in peanuts. Thrips were also controlled. Control of ring nematodes, however, was reported as poor. Yield increases were found to be directly related to control of the root-knot nematode; little relation was found between thrips control and yield.

Most test plots produced significant yield increases of peanuts when treated with carbofuran. Compared to untreated plots, yield changes varied from a loss of 412 lb/acre to a gain of 2,258 lb/acre. Economic benefits ranged from a loss of $70.70/acre to a gain of $293.00/acre.

Potatoes - Carbofuran was found to be effective against potato infestation caused by the Colorado potato beetle, wireworms, flea beetles, and aphids. Control was effective for several weeks, with 1 application at rates varying from 0.5 to 8.0 lb/acre. Yields increased significantly in all but one test. Compared to untreated plots, yields varied from a loss of 21 cwt/acre to a gain of 213 cwt/acre. Economic benefits ranged from a loss of $83.50/acre to a gain of $625.00/acre.

Rice - Carbofuran was found to be effective in controlling the rice water weevil for up to 6 weeks. Applications made as preplant or up to 5 weeks after flood were effective. Control of mosquito larvae was reported as excellent with carbofuran. Rice yields generally increased with the use of carbofuran. Compared to untreated test plots, yields ranged from a loss of 214 lb/acre to a gain of 1,302 lb/acre. Economic benefits ranged from a loss of $24.60/acre to a gain of $106.50/acre.

Tobacco - Carbofuran is used for control of wireworms and the hornworm in tobacco. It is also reported to be effective in control of the tobacco budworm and tobacco flea beetle. Control of the hornworm was achieved for 7 weeks after 1 application. Better control of the budworm was achieved at 4.0 to 6.0 lb/acre than at lower rates. Control of the flea beetles was greatest with a pretransplant application followed by a posttransplant application. Tobacco yield changes ranged from 152 to 161 lb/acre compared to untreated plots. Economic benefits varied from $102.00 to $110.00/acre.

Peppers - Carbofuran is recommended for control of the green peach aphid and European corn borer in peppers. Two applications were successful in controlling the borer. Yields increased in all tests reviewed, and some were significantly better than untreated test plots. Yield changes varied from a gain of 22 cwt to 82 cwt/acre, compared to untreated test plots. Economic benefits range from $269.00 to $1,035.00/acre.

Sugarcane - Carbofuran is considered effective for controlling the sugarcane borer and wireworms. It also is used in control of nematodes, and it significantly increases sugarcane yields. Economic benefits, based on one test, were $410.00/acre.

PART II. INITIAL SCIENTIFIC REVIEW

SUBPART A. CHEMISTRY

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This section contains a detailed review of available data on carbofuran's chemistry and presence in foods. Eight subject areas have been examined: Synthesis and Production Technology; Physical Properties of Carbofuran; Analytical Methods; Composition and Formulation; Chemical Properties, Degradation Reactions and Decomposition Processes; Occurrence of Residues in Food and Feed Commodities; Acceptable Daily Intake; and Tolerances. The section summarizes rather than interprets data reviewed.

Synthesis and Production Technology

Carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate) is manufactured by the Agricultural (formerly Niagara) Chemical Division of the FMC Corporation. FMC's manufacturing plant for carbofuran is located at Middleport, New York, but an important intermediate of carbofuran (2,3-dihydro-2,2-dimethyl-7-benzofuranol) is produced at Baltimore.

The process used for manufacturing carbofuran (FMC, 1975), is described in patents by Borivoj (1967) and Thorpe (1974). The reactions for this process are shown in Figure 2. A schematic diagram of this process is shown in Figure 3.

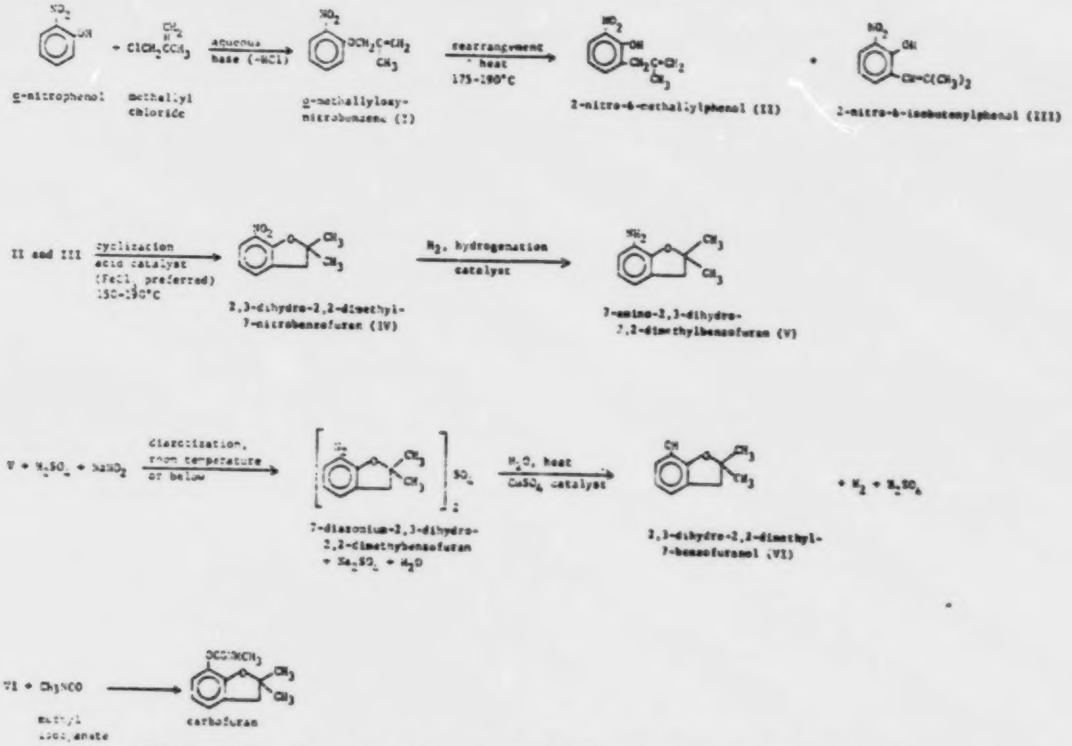

o-nitrophenol
methallyl chloride
aqueous base (-HCl)
o-methallyloxy-nitrobenzene (I)
rearrangement heat 175-190°C
2-nitro-6-methallylphenol (II)
2-nitro-6-isobutenylphenol (III)
II and III
cyclization acid catalyst (FeCl$_3$ preferred) 150-190°C
2,3-dihydro-2,2-dimethyl-7-nitrobenzofuran (IV)
H$_2$, hydrogenation catalyst
7-amino-2,3-dihydro-2,2-dimethylbenzofuran (V)
V + H$_2$SO$_4$ + NaNO$_2$
diazotization, room temperature or below
7-diazonium-2,3-dihydro-2,2-dimethylbenzofuran + Na$_2$SO$_4$ + H$_2$O
H$_2$O, heat
CuSO$_4$ catalyst
+ N$_2$ + H$_2$SO$_4$
2,3-dihydro-2,2-dimethyl-7-benzofuranol (VI)
VI + CH$_3$NCO
methyl isocyanate
carbofuran

Figure 2. Preparation of Carbofuran from o-Nitrophenol

Source: FMC (1975).

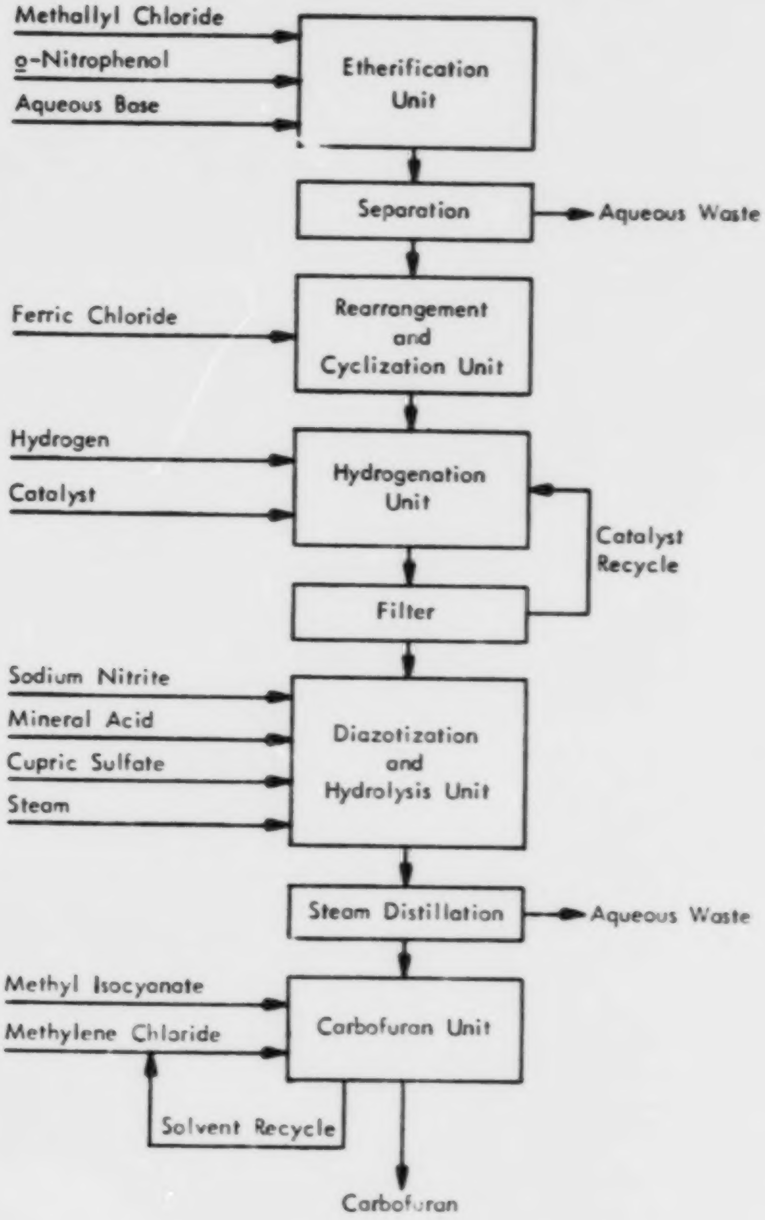
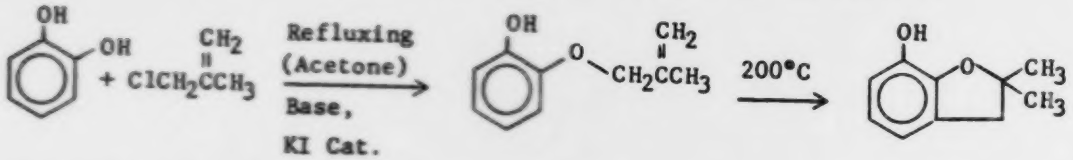


Figure 3. Production Schematic for Carbofuran

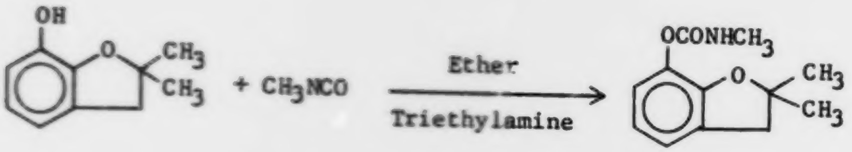
Source: FMC (1975).

An alternate manufacturing process for carbofuran is described by Scharpf (1969). The reactions for this process are as follows:



(1)

Catechol Methallyl chloride Methallyloxyphenol 2,3-Dihydro-2,2-dimethyl-7-benzofuranol

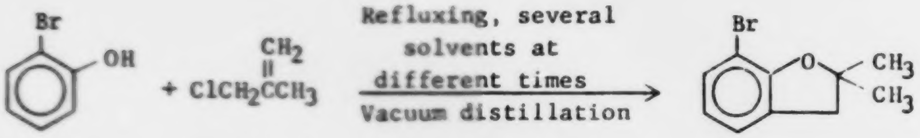


(2)

Methyl Isocyanate Carbofuran

In the laboratory preparation described in the Scharpf patent, the yield in the step from catechol to methallyloxyphenol was 44%. The yield for Reaction (2) was 73%. The overall yield could not be calculated from the data given.

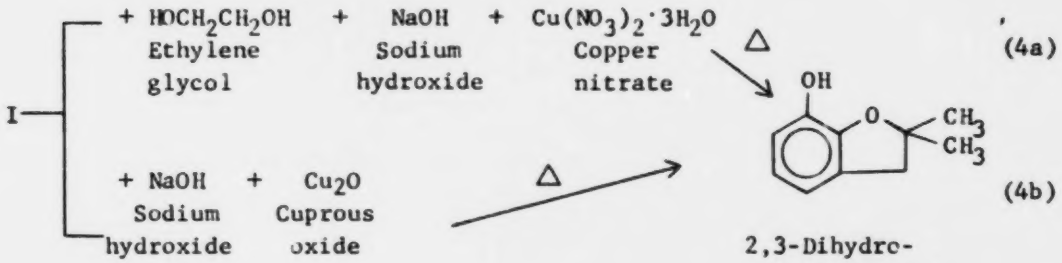
Several other patents issued to FMC describe processes for the manufacture of the intermediate 2,3-dihydro-2,2,-dimethyl-7-benzofuranol. These processes are described below. Orwoll (1967) describes a process beginning with o-bromophenol as shown in Equations (3), (4a), and (4b).



(3)

o-Bromophenol Methallyl chloride

2,3-Dihydro-2,2-dimethyl 7-bromobenzofuran (I)



2,3-Dihydro-
2,2-dimethyl-
7-benzofuranol

Before the patent to Scharpf (1969) was issued, Borivoj (1967) reported that catechol is an expensive starting material compared to o-nitrophenol. Furthermore, the overall yield from o-nitrophenol was reported to be high, about 50% based upon o-nitrophenol, even though the process involved many steps. (See Figure 2.)

Physical Properties

Chemical name: 2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate

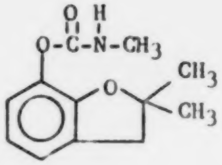
Common name: Carbofuran

Other names: Furadan®, NIA 10242, ENT 27164

Pesticide class: Insecticide, acaricide, nematicide; carbamate

Empirical formula: $C_{12}H_{15}NO_3$

Structural formula:



Molecular weight: 221.3

Elemental analysis: C, 65.2%; H, 6.8%; N, 6.3%; O, 21.7%

Physical state: White, crystalline solid

Odor: Odorless (Martin, 1971)
Slightly phenolic (FMC, 1971b)

Density: 1.180 at 20/20°C

Melting point: Pure, 153 to 154°C
Technical, 150 to 152°C
Degrades at temperatures in excess of 130°C (FMC, 1971b)

Vapor pressure: 2×10^{-5} mm Hg at 33°C
1.1×10^{-4} mm Hg at 50°C

Solubility: % weight/weight, 25°C (Cook, 1973)

Acetone	15
Acetonitrile	14
Benzene	4
Cyclohexanone	9
Dimethyl formamide	27
Dimethyl sulfoxide	25
Ethanol	4
Kerosene	< 1
N-Methyl-2-pyrrolidone	30
Methyl chloride	12
Petroleum ether	< 1
Xylene	< 1
Water	0.07 (700 ppm)

Carbofuran is essentially insoluble in conventional formulation solvents employed in agriculture (FMC, 1971b).

Flammability: Not flammable--will support combustion if ignited.

Explosive hazard: Nonhazardous at normal temperatures

Corrosive action: Noncorrosive

Analytical Methods

This subsection reviews analytical methods for carbofuran. The review describes multi-residue methods, residue analysis principles, and formulation analysis principles. Information on the sensitivity and selectivity of the methods is also presented.

Multi-Residue Methods - Carbofuran cannot be detected by the multi-residue methods described in the Pesticide Analytical Manual (PAM, Vol. I, 1971); it is not obtained in the eluate from the extraction and cleanup procedures.

A procedure has recently been developed by Holden (1973) that can be used for several methylcarbamate pesticides in plant materials. The procedure calls for extraction of the crop material with acetonitrile, then partitioning the extract with petroleum ether. The extract is purified by means of a coagulation procedure using phosphoric acid-ammonium chloride solution. The mixture is filtered through celite and the filtrate is extracted with methylene chloride. Phenolic impurities are eliminated by partitioning the methylene chloride extract with 0.1 N potassium hydroxide. The residue, after evaporation of the methylene chloride, is treated with 1-fluoro-2,4-dinitrobenzene to form an ether derivative. Conversion in this step is essentially complete. Determination is then made by electron capture gas chromatography. Residues may be determined as low as 0.05 ppm, with recoveries between 90 and 110%. This procedure, however, will not detect phenolic metabolites or plant metabolic conjugates such as the 3-hydroxycarbofuran glycosides.

Residue Analysis Principles - There is one basic method for carbofuran residue analysis. It employs microcoulometric gas chromatography with a nitrogen detection system. The most important studies all use this basic method, although there are changes in extraction and cleanup procedures for specific food products. The method was first published by Cook et al. (1969). The method is also described in PAM (Vol. II, 1967) and in Residue Reviews (Cassil et al., 1969). Cook (1973) has summarized previous reports for carbofuran in 40 products, including various plant materials, animal materials, milk, water, and soil (Table 1). The details of the extraction methods are described below. The following diagram shows the steps in this method (McCarthy, 1970).

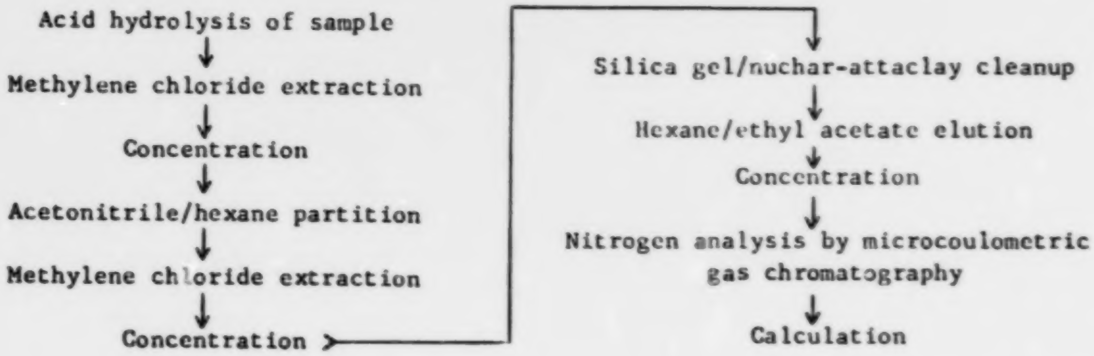

Acid hydrolysis of sample
Methylene chloride extraction
Concentration
Acetonitrile/hexane partition
Methylene chloride extraction
Concentration
Silica gel/nuchar-attaclay cleanup
Hexane/ethyl acetate elution
Concentration
Nitrogen analysis by microcoulometric gas chromatography
Calculation

Table 1. Method Requirements for Specific Samples

Sample	Sample size (g)	Partition	Column cleanup: Muchar-attaclay (g): packing (g)	Column cleanup: ml Ethyl acetate/ hexane (v/v)	Method sensitivity (ppm)
Alfalfa	25	No	7: 10 silicic acid	125-70/30	0.20
Alfalfa, hay	5	No	7: 10 silicic acid	125-70/30	0.20
Apples	50	No	7: 5 silica gel	100-70/30	0.10
Beans, green	50	Yes	7: 5 silica gel	100-70/30	0.10
Beans, lima	50	Yes	7: 5 silica gel	100-70/30	0.10
Carrots	100	No	7: 5 silica gel	300-70/30	0.05
Corn, cobs	50	No	7: 5 silica gel	100-70/30	0.10
Corn, grain	70	Yes	7: 5 silica gel	100-70/30	0.10
Corn, husks	50	Yes	7: 5 silica gel	150-80/20	0.10
Corn, silage	50	Yes	7: 5 silica gel	150-80/20	0.10
Corn, stover	50	No	7: 5 silica gel	100-70/30	0.10
Eggs	100	Yes	7: 5 silica gel	150-70/30	0.05
Lettuce	50	No	7: 10 silicic acid	125-70/30	0.20
Milk	100	Yes	7: 5 silica gel	150-70/30	0.025
Peaches	50	No	7: 5 silica gel	100-70/30	0.10
Peanut, hay	100	Yes	5: 10 Florisil[a]	100-80/20	0.5
Peanut, hulls	20	No	5: 10 Florisil[a]	100-80/20	0.1
Peanut, vines	20	Yes	5: 10 Florisil[a]	100-80/20	0.5
Peanuts	40	No	5: 10 Florisil[a]	100-80/20	0.1
Pears	50	No	7: 5 silica gel	100-70/30	0.1
Peppers, green	100	Yes	7: 5 silica gel	200-70/30	0.05
Potatoes	100	No	5: 10 Florisil	150-70/30	0.05
Pumpkins	50	Yes	7: 5 silica gel	100-70	0.10
Rice, grain	20	Yes	3: 15 Florisil[b]	230-100/0	0.20
Rice, hulls	20	Yes	3: 15 Florisil[b]	230-100/0	0.20
Rice, green straw	40	No	3: 15 Florisil[b]	230-100/0	0.20
Rice, dry straw	10	Yes	3: 15 Florisil[b]	230-100/0	0.20
Soil	50	No	7	150-80/20	0.10
Sugar beets, foilage	50	No	7: 10 aluminum oxide[c]	125-100/0[d]	0.10
Sugar beets, pulp	20	No	7: 10 aluminum oxide[a]	125-100/0	0.10
Sugar beets, roots	50	No	7: 10 aluminum oxide[a]	125-100/0	0.10
Sugar cane	40	No	5: 10 Florisil[a]	100-60/40	0.10
Sugar cane juice	40	No	5: 10 Florisil[a]	100-60/40	0.10
Tissue, gizzards	100	No	7	150-80/20	0.05
Tissue, kidney	100	Yes	7: 5 silica gel	150-70/80	0.05
Tissue, liver	100	Yes	7: 5 silica gel	150-70/80	0.05
Tissue, muscle	100	Yes	7: 5 silica gel	150-70/80	0.05
Tobacco, dry	10	No	7: 10 silicic acid	125-70/80	0.20
Tobacco, green	50	No	7: 10 silicic acid	125-70/80	0.20
Tomatoes	50	No	5: 10 Florisil	100-80/20	0.05
Water	100	No	5: 10 Florisil	110-80/20	0.01

---

[a] Concentrate the dried methylene chloride extract (1,800 ml) in a Kuderna-Danish evaporator to about 10 ml. Transfer the concentrate to a 20-ml beaker containing 1 g of Florisil. Rinse the evaporator ampoule with 3 ml of methylene chloride. Air-dry the sample onto the Florisil with occasional mixing. Transfer the 1-g Florisil sample to the top of the cleanup column, rinse the beaker with some elution solvent, and proceed with the specified elution.

[b] In preparing the cleanup column, place 15 g of anhydrous sodium sulfate between the adsorbent layers and another 15 g as a top cap.

[c] In preparing the cleanup column, place 10 g of anhydrous sodium sulfate between the adsorbent layers and another 10 g as a top cap.

[d] Add the dried methylene chloride sample extract (135 ml) to the cleanup column and allow the solvent level to reach the top of the sodium sulfate layer. Add 150 ml of hexane and allow it to drain to the top of the sodium sulfate. Discontinue suction and discard all previously eluted [illegible] with the listed solvent system.

Source: Adapted from [illegible].

Cook (1973) described extraction methods for plant materials as follows:

> Place the appropriate amount of chopped and blended crop in a 1,000-ml round-bottomed flask containing a magnetic stirring bar. Add 600 ml of 0.25 N hydrochloric acid. Connect the round-bottomed flask to a Liebig condenser using a 50/50 to 24/40 ₸ neck adapter. Reflux the crop-acid mixture for 1 hr using a heating mantle. Swirl the flask contents by hand during the initial heating period and then continuously stir the mixture with a magnetic stirring bar. Fortify check crop samples prior to the addition of acid.
>
> After 1 hr of refluxing, remove the round-bottomed flask from the heating mantle and filter the hot sample through glass wool into a 1,000-ml Erlenmeyer flask. Wash the reflux flask and glass wool with an additional 300 ml of hot 0.25 N hydrochloric acid. Cool the filtrate for 1 hr at -10°C and transfer into a 2,000-ml separatory funnel. Add approximately 250 mg of sodium lauryl sulfate to the filtrate and mix. Extract the aqueous phase 3 times with 600 ml of distilled methylene chloride. Combine the methylene chloride extracts and dry over anhydrous sodium sulfate.

A modification of this procedure which is suitable for residues in small fruits is reported in Williams and Brown (1973).

Cook (1973) described extraction methods for milk as follows:

> Pour 100 ml (100 g) of milk into a blender. Add 500 ml of distilled acetone and blend for 3.0 min. Fortify check milk samples prior to the addition of acetone. Filter the sample in a 1,000-ml round-bottom flask. Add 100 ml of 0.375 N hydrochloric acid and 2 or 3 glass beads. Connect a Snyder column to the flask. Place the sample mixture in the steam bath and evaporate all the acetone, leaving the sample in the aqueous solution. Reflux the aqueous solution for 15 min. Remove the round-bottom flask from the steam bath and rinse the bubble column with 0.375 N hydrochloric acid. Place the aqueous solution in a freezer (-10°C). Allow the sample to cool until ice just begins to form (about 1.5 hr). Remove the sample from the freezer and filter quickly through glass wool into a 1,000-ml separatory funnel to remove any oils or waxes which have solidified during cooling. Rinse the round-bottom flask and glass wool with about 50 ml of 0.375 N hydrochloric acid. Extract the aqueous phase 3 times with 200 ml of distilled methylene chloride. Combine the methylene chloride extracts and dry over anhydrous sodium sulfate.

Cook (1973) described extraction methods for animal material as follows:

> Place the appropriate amount of subsampled diced tissue or eggs (shells removed) into a blender. Add 300 ml of acetone and blend for 3.0 min. Filter the blended mixture through a Buchner

> funnel, using No. 5 filter paper. Retain the filtrate. Return the filter paper and the tissue residue to the blender. Add 300 ml of acetone and blend again for 30 min. Filter the blended mixture through a Buchner funnel using No. 5 filter paper. Combine the first and second filtrates.
>
> Allow the combined filtrates to stand in a 1,000-ml separatory funnel for 0.75 hr. Drain off any oils that settle to the bottom. (Note: Beef tissue and egg filtrate "oil" will settle out at room temperature. Chicken tissue filtrate may require cooling to settle out the "oil.")
>
> Place the acetone filtrate from above into a 1,000-ml round-bottom flask (24/40 ₮ neck) with a few glass beads. Connect a Snyder column to the flask and concentrate the acetone to approximately 50% of its initial volume on a steam bath. Remove the flask from the steam bath and add 150 ml of 0.25 N hydrochloric acid. Replace the sample mixture in the steam bath and evaporate all the acetone. Reflux the aqueous solution for an additional 0.25 hr to insure complete conversion of the conjugated residues to the aglycone form. Remove the round-bottom flask from the steam bath. Rinse the bubble column with 0.25 N hydrochloric acid. Place the aqueous solution in a freezer (-10°C) for 1.5 hr to allow the remaining fats and oils to solidify. Remove the sample from the freezer and quickly filter through a small bed of glass wool into a 500-ml separatory funnel. Rinse the flask and glass wool with 50 ml of 0.25 N hydrochloric acid. Extract the filtrate 3 times with 100-ml portions of methylene chloride. Combine the methylene chloride extract and dry over anhydrous sodium sulfate.

Cook (1973) described extraction methods for water as follows:

> Place the appropriate amount of subsampled water into a 250-ml separatory funnel. Extract 3 times with 100-ml portions of methylene chloride. Combine the methylene chloride extracts, dry over sodium sulfate, and filter. Wash the sodium sulfate and filter paper with methylene chloride.

Formulation Analysis - The recommended method for analysis of carbofuran formulations is by gas chromatography, using an internal standard, comparing the peak area of the unknown sample to the peak area of the standard (Cook, 1973). Other analytical methods for identification and/or reference are infrared spectrometry (Chen and Benson, 1966); nuclear magnetic resource spectrometry, (Keith and Alford, 1970), and spectrometry (Vickers et al., 1973).

Other Residue Methods - Table 2 lists other analytical methods and sensitivities.

Table 2. Other Analytical Methods for Carbofuran Residues

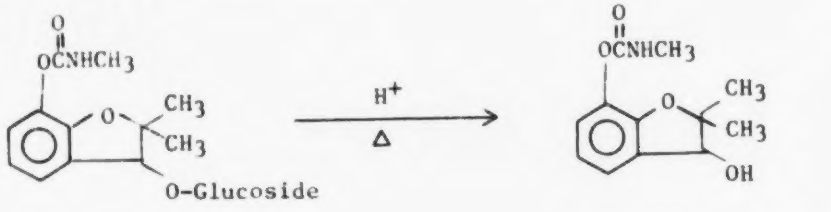
Type of method	Sensitivity	Source
Spectrophotofluorometry	0.5 ppm	Bowman and Beroza (1967b)
Gas liquid chromatography Alkaline hydrolysis to phenol, steam distillation and derivitization as thiophosphoryl ether followed by fluoro photometric detection in phosphorous mode.	0.04 ppm	Bowman and Beroza (1967a)
Infrared analysis	50 μg	Broderick et al. (1966)
Electron-capture gas chromatography of trichloroacetates after hydrolysis of carbofuran residues to phenols	0.01-0.10 ppm	Butler and McDonough (1968)
Electron-capture gas liquid chromatography of trichloroacetates of carbamates after removal of phenolic metabolites	0.01 ppm	Butler and McDonough (1971)
Electron-capture gas chromatography of dinitrophenyl ethers	0.1 ppm	Caro et al. (1973b)
High-speed liquid chromatography	2-10 ng/injection	Frei et al. (1974)
Electron-capture gas chromatography	-	Holden et al. (1969)
Thin-layer chromatography-spectrophotofluorometry	ppb range	Lawrence and Frei (1972b), Lawrence and Frei (1972a), Lawrence et al. (1972)
Thin-layer chromatography-enzyme inhibition	-	Mendoza (1972), Mendoza and Shields (1970), Mendoza and Shields (1971)
Thin-layer chromatography	ng range	Winterlin et al. (1968)
Phosphorescence	-	Moye and Winefordner (1965)

Table 2. Other Analytical Methods for Carbofuran Residues (Continued)

Type of method	Sensitivity	Source
Gas chromatography of N-perfluoroacyl derivatives	-	Seiber (1972)
Electron-capture gas chromatography of various ether derivatives	-	Seiber et al. (1972)
Transesterification with methanol via reaction gas chromatography to form methyl N-methylcarbamate with alkali flame detection	0.05 ppm	Van Middlelem et al. (1971)
Spectrometry (laser excited Ramen and fluorescence spectra)	-	Vickers et al. (1973)
Gas chromatography (Review article)	-	Williams (1970)

In addition to carbofuran itself, 2 types of metabolites are detected by the method of Cook (1973). These are 3-hydroxycarbofuran and various conjugated forms of 3-hydroxycarbofuran including glycosides (plant metabolic conjugates) and glucuronides (conjugated products of animal metabolism).

The water-soluble conjugated forms are converted into the 3-hydroxycarbofuran (aglycone) form before extraction. The equation for this acid hydrolysis reaction is as follows (Cook, 1973):



3-Hydroxyglucoside

3-Hydroxycarbofuran

It should be noted that some of the methods listed in Table 2 are not applicable to the conjugated forms because organic solvent extraction techniques were used that did not remove the water-soluble conjugated form. These were the methods of Bowman and Beroza (1967a) and Butler and McDonough (1968).

In addition, Kuhr and Casida (1967) and Metcalf (1968) indicate that certain glycosidic conjugates are difficult to cleave to corresponding aglycone.

More recently an analytical method has been developed to detect the phenolic metabolites of carbofuran. These metabolites are carbofuran phenol, 3-ketocarbofuran-7-phenol, and 3-hydroxycarbofuran-7-phenol. The method consists of hydrolyzing possible conjugates, deriving the 3-hydroxy moiety to the ethoxy or n-propoxy ether and then deriving the phenol to the 2,4-dinitrophenyl ether. Analysis is by GC, using a nitrogen-specific detector (FMC,1971a). Its application to potato tubers, milk, eggs, and cattle and poultry tissue are reported by Jackson (1973a and 1973b) and Shuttleworth (1973).

It should be noted that all current tolerances include consideration of both phenolic metabolites (and conjugates) as well as oxidation products still containing the carbamate functional grouping (see p. 34).

Occurrence of Residues in Food and Feed Commodities

Methods for detecting residues in crops are described in the subsection on Analytical Methods (see p. 21). Residue tests for various crops are described below.

Sugarcane - Carbofuran was applied to sugarcane grown in 7 locations in Florida and Louisiana. Twenty-seven test plots treated with 3 and 4 applications of carbofuran 3G (total of 3 to 4 lb AI/acre) were sampled at post-harvest intervals ranging from 0 to 55 days. There were only 3 instances in which the total residues from the 4 lb AI/acre rate measured 0.1 ppm or greater. In one test, at 0 days from last application to harvest, 0.23 ppm residues were found. In a second test, 18 days after the harvest, residues ranged from 0.1 to 0.2 ppm. In a third test, also 18 days after the harvest, 0.37 ppm residues were found.

Carbofuran 10G applied at rates to 32 lb AI/acre, with post-harvest intervals ranging from 212 to 427 days, resulted in no detectable residues.

Applications of carbofuran 75 WP produced variable results, as shown, with other applications in the following table (FMC, 1969a).

Table 3. Residues of Carbofuran on Sugarcane[a]

Formulation	Active ingredient per application (lb/acre)	Number of applications	Days from last application to harvest	Total residue[b] (ppm)
10G	8	1	356	ND
10G	8	1	356	ND
10G	8	2	212	ND
10G	8	2	212	ND
75 WP[d]	0	0		ND
75 WP	0.6	4	2	1.03
75 WP	0.6	4	2	0.5 to 0.6
75 WP	0.6	4	17	< 0.1
75 WP	0.6	4	17	< 0.1
75 WP	0.6	4	33	< 0.1
75 WP	0.6	4	33	< 0.1
75 WP	1.2	4	2	0.83
75 WP	1.2	4	2	0.48
75 WP	1.2	4	17	0.11
75 WP	1.2	4	17	0.11
75 WP	1.2	4	17	< 0.1
75 WP	1.2	4	33	< 0.1
75 WP	1.2	4	33	ND
3G	0	0		ND
3G	0.9	4	0	0.23
3G	0.9	4	0	< 0.1
3G	0.9	4	18	0.1 to 0.20
3G	0.9	4	18	0.37
3G	0.9	4	41	ND
3G	0.9	4	41	< 0.1
3G	0.45	3	55	ND
3G	0.45	3	55	ND

---

[a] Data from seven locations in states of Florida and Louisiana.

[b] Total residue equals carbofuran plus 3-hydroxycarbofuran. The analytical method used was microcoulometric gas chromatography with a nitrogen detector, corrected for recovery.

[c] ND = None detectable.

[d] Formulation currently not available.

Source: FMC (1969a).

Corn Fields - Table 4 summarizes data for carbofuran tests on field corn grown in 4 states.

Table 4. Maximum Total Residues (ppm of Carbofuran Including 3-hydroxycarbofuran) Found on Field Corn Silage and Stover

		AI/acre			
Days lapsed	Location	1 lb rate	2 lb rate	4 lb rate	8 lb rate
75	Arkansas			1.0	7.3
76	Arkansas	3.0 (0.8)[a]	5.1 (3.9)	4.6 (1.9)	
92	New York			2.4	
98	Iowa			0.5	
101	Nebraska			1.3	
111	New York			3.1	
133	Arkansas			0.8	2.8
133	Iowa			0.1	
136	Nebraska			0.4	

---

[a] Values in parentheses are from the banded treatment (7-in band/40-in row). All others are in-furrow, 10G formulation.

Note: Carbofuran was found to be nondetectable in corn grain at rates to 8 lb/acre harvested from 111 to 133 days after application. The maximum recommended application rate is 3 lb AI/acre.

Source: FMC (1971a).

Alfalfa - Dissipation studies (FMC, 1968) were conducted on alfalfa grown in 9 states with carbofuran applied at levels ranging from 0.25 to 2.0 lb AI/acre. Total carbamate residues were determined on green alfalfa by a nitrogen specific microcoulometric gas chromatograph method sensitive to 0 2 ppm carbofuran and 0.2 ppm of the metabolite 3-hydroxycarbofuran. Only carbofuran, 3-hydroxycarbofuran, and 3-hydrocarbofuran glucoside were found. The glucoside was hydrolized quantitatively and reported as 3-hydroxycarbofuran. All results were adjusted for 80% moisture in the alfalfa.

Wide variations were found in residue dissipation due to the combined effect of various factors including climatic conditions, metabolism in the plant, rate of growth, density, and uniformity of the stand. Maximum total carbamate residues in ppm were as follows:

Table 5. Residues of Carbofuran in Alfalfa
(ppm AI/acre)

Days	0.25	0.50	1.0	2.0
0	15.5	32.4	114.0	145.5
7	0.9	20.6	48.5	87.0
14	0.5	3.8	6.6	11.4
21	--	1.4	7.4	8.2
28	0.5	1.0	4.1	--

Source: FMC (1968).

In some of the studies, samples of alfalfa hay were taken to compare residue values with those in the green alfalfa of the same time interval. Water determination gave an average of 16% in the hay. A drying method, reducing the moisture from 80% to 15%, would give a factor of 4.25; this theoretical factor was verified by tests on the green and dried samples of the same interval cuttings. Studies from 9 states with carbofuran applied at 1.0 lb AI/acre showed total residues ranging from 1.4 to 14.5 ppm at zero day and 4.1 to 0.1 ppm AI/acre 28 days posttreatment.

A study was made on the persistence of carbofuran and 3-hydroxycarbofuran on alfalfa in Massachusetts. When carbofuran was applied to first-cutting alfalfa at the rate of 0.5 lb AI/acre, no detectable residue of carbofuran was found in the green plant 21 days posttreatment; 3-hydroxycarbofuran amounted to 0.55 ppm. At 1.0 lb AI/acre, the carbofuran residue was below the sensitivity of the method and the metabolite was measured at 1.26 ppm 21 days posttreatment. Stubble sprays of carbofuran at 0.5 and 1.0 lb AI/acre resulted in no detectable residues of carbofuran and a maximum of 1.5 ppm of the metabolite on the dry hay (Shaw et al., 1969).

Studies of Fahey (1970) on green and dehydrated alfalfa grown in South Dakota and treated with carbofuran at 0.5 and 1.0 lb AI/acre showed no measurable residues of carbofuran in samples collected 14 and 21 days after treatment. The loss of carbofuran attributed to dehydration averaged 67% for plots treated with 1.0 and 0.5 lb AI/acre and sampled the same day.

Rice - Test data was obtained from rice grown in California, Louisiana, and Texas (FMC 1969b). When carbofuran was applied as a 2 G formulation at rates from 0.5 to 2.0 lb AI/acre, green straw rice harvested from 25 to 148 days after application contained less than 0.3 ppm carbofuran residues.

Whole grain rice grown on soil treated with carbofuran 2G at rates of 0.5 to 2.0 lb AI/acre and harvested from 110 to 168 days after application likewise contained less than 0.3 ppm carbofuran residues, with the majority of samples containing less than 0.2 ppm. Similar results were obtained when carbofuran 3G was applied at 0.5 to 1.0 lb AI/acre, with a post-harvest interval of only 51 days. Hulls, polishings, broken grains, and polished grain from rice harvested 87 to 92 days after applications of carbofuran 3G at 0.5 to 1.0 lb/acre contained less than 0.3 ppm residues.

Total residues equaled carbofuran plus 3-hydroxycarbofuran. The analytical method used was microcoulometric gas chromatograph (MCGC), with a nitrogen detector corrected for recovery. It should be noted that, even on samples taken from rice receiving no treatment, residues were reported as <0.2 ppm.

Peanuts - Table 6 lists the data obtained from tests of carbofuran on peanuts (FMC,1970). The data listed includes portions of plant, type of application, amount of active ingredient applied per acre, days lapsed, and total residue of carbofuran plus 3-hydroxycarbofuran. The maximum residue in the nut portion was less than 0.1 ppm. The maximum residue in the hulls was 0.8 ppm. The maximum residues in the vines by type of application were: banded at planting, 1.5 ppm; in-furrow at planting, 20 ppm; banded at pegging, 9 ppm; and in-furrow at planting plus banded at pegging, 37 ppm.

General - A study (Shuttleworth, 1974) was conducted to determine whether or not a buildup of residues of carbofuran and its metabolite 3-hydroxycarbofuran would occur in raw agricultural commodities (corn, potatoes, peanuts, and tobacco) grown on plots treated 4 consecutive years with carbofuran at registered or proposed rates and use patterns. Plots were located in the south, midwest, and east. Samples were analyzed by a nitrogen specific microcoulometric gas chromatograph. Depending upon the crop, method sensitivities ranged from 0.075 ppm to 0.20 total carbamates. Recoveries exceeded 70% for both carbofuran and the metabolite.

Potato tubers grown in New York and receiving 5 foliar applications of carbofuran 4F at 1.0 lb AI/acre yielded no carbamate residues approaching the sensitivity of the method.

Corn grown in Nebraska and New York on soils treated with carbofuran 10G (in-furrow and banded) at 3.0 lb AI/acre contained no detectable residues in either grain or stalk samples from either location.

Peanuts grown in Arkansas on soil treated with 1.0 and 2.0 lb AI/acre (as carbofuran 10G) in-furrow and at pegging, respectively, showed trace residues (0.025 ppm) of carbofuran and 20.10 ppm of 3-hydroxycarbofuran.

Tobacco samples from Arkansas plots treated with 6.0 lb AI/acre carbofuran 10G broadcast yielded total carbamate residues of 0.13 ppm. Previous samples yielded up to 15.0 ppm after 3 yr of consecutive treatments. High variability from plot to plot was indicated because re-analyses verified prior results.

Table 6. Residues of Carbofuran on Peanuts[a]

Portion of plant	Type of application	Active ingredient (lb/acre)	Days lapsed	Total residue[b] (ppm)
Nuts	14-in band	2	166	ND[c]
Hulls	on 42-in row			< 0.20
Vines	at planting			NA[d]
Nuts	18-in band	4	139	ND
	on 36-in row			< 0.10
Hulls	at planting			0.26
				0.33
Vines				1.33
				1.47
Nuts	In-furrow at	1	153	ND
	planting			ND
Hulls				0.81
				0.59
Vines				15.6
				11.9
Nuts	In-furrow at	1	123	ND
	planting			ND
Hulls		1	123	0.36
				0.32
Vines		1	123	4.1
				20.3
Nuts	In-furrow at	3	123	< 0.10
	planting			ND
Hulls				0.69
Vines				37.2
				38.8
Nuts	12-in band	2	92	ND
	on 36-in row			ND
Hulls	at pegging			NA
Vines				9.09
				8.54

Table 6. (Continued)

Portion of plant	Type of application	Active ingredient (lb/acre)	Days lapsed	Total residue[b] (ppm)
Nuts	12-in band on 36-in row at pegging	2	79	< 0.10 ND
Hulls				0.62 0.67
Vines				< 1.43, > 0.93 1.63
Nuts	Dual-in-furrow at plant plus banded at pegging	1 and 2	74	< 0.10 < 0.10
Hulls				0.71
Vines				36.6 34.5

---

a/ Data from five locations in Florida, Georgia, Mississippi, North Carolina, and Virginia.

b/ Total residue equals carbofuran plus 3-hydroxycarbofuran. The analytical method used was microcoulometric gas chromatography with a nitrogen detector, corrected for recovery.

c/ ND = None detectable.

d/ NA = Not available or not analyzed.

Source: FMC (1970).

It was concluded that carbamate residues above existing or proposed tolerances would not occur from annual treatments with carbofuran at registered or proposed rates.

Meat and Milk - Reno (1973b) fed 3 phenolic metabolites of carbofuran to cows at a dietary level of 200 ppm. The 3 metabolites were carbofuran phenol, 3-keto-7-phenol-carbofuran and 3-hydroxy-carbofuran phenol. Equal quantities of each metabolite were fed and the dietary levels were 20, 60, and 200 ppm total metabolites.

The results of the milk residue study are shown in Table 7. Table 7 shows the results of the 200 ppm study. The results for the average level (of the 4 cows) and the maximum level are given for 2 of the metabolites. The third metabolite, 3-hydroxy-7-phenol carbofuran, was not detectable (Shuttleworth, 1973).

The results of tissue analyses from this study are shown in Table 8. The tissue was taken by sacrificing 2 of the test animals at the end of the 28-day feeding period.

Reno (1973a) conducted a similar feeding test with chickens. Test animals were fed 2, 6, and 20 ppm total metabolites (one-third each metabolite). Egg and tissue (liver, fat, and breast) samples from the 20 ppm study were analyzed by the FMC Corporation using a gas chromatograph equipped with a nitrogen specific Coulson conductivity detection system (Shuttleworth, 1973). No phenolic residues were detected at or above 0.05 ppm (method sensitivity).

Other residue data related to carbofuran and its metabolites in milk and tissue samples from domestic ruminants is discussed in the subsection on tolerances.

Acceptable Daily Intake

The acceptable daily intake (ADI) is defined as the daily intake which, during an entire lifetime, appears to be without appreciable risk on the basis of all known facts at the time of evaluation (Lu, 1973). It is expressed in milligrams of the chemical per kilogram of body weight (mg/kg).

The ADI for pesticides is established jointly by the Food and Agricultural Organization (FAO) Committee on Pesticides in Agriculture and the World Health Organization (WHO) Expert Committee on Pesticide Residues. However, an ADI for carbofuran has not yet been established.

Tolerances

The tolerances for carbofuran apply to the total of carbofuran plus the following 4 metabolites: 3-hydroxycarbofuran (2,3,-dihydro-2,2-dimethyl-3-hydroxy-7-benzofuranyl-N-methylcarbamate), structure II, p. 38; carbofuran phenol (2,3-dihydro-2,2-dimethyl-7-benzofuranol), structure VII, p. 38; 3-hydroxycarbofuran phenol (2,3-dihydro-2,2-dimethyl-3,7-benzofurandiol), structure IX, p. 38; and 3-ketocarbofuran phenol (2,3-dihydro-2,2-dimethyl-3-oxo-7-benzofuranol), structure VIII, p. 38.

Official pesticide tolerances are published in the Code of Federal Regulations, Title 40, and updated in the Federal Register. A summary of current tolerances for carbofuran is presented in Table 9. A distinction is made between residues containing a carbamate function (cholinesterase-inhibiting compounds) and those without this function. Tolerances are based upon the assumption that complete hydrolysis of all conjugates has taken place prior to analysis.

Table 7. Residues in Milk of 3 Metabolites of Carbofuran Fed at 200 ppm Total Metabolites[a]

	Residue, ppm[b]			
	Carbofuran phenol		3-Keto-7-phenol carbofuran	
Days lapsed	Average[c]	Maximum	Average	Maximum
Pretest (0)	ND[d]	ND	ND	ND
2	0.044	0.057	0.44	0.49
4	0.043	0.069	0.36	0.55
7	0.025	0.034	0.37	0.48
14	0.030	0.047	0.41	0.59
18	0.049	0.060	0.58	0.77
21	0.052	0.065	0.49	0.70
25	0.046	0.057	0.55	0.71
28	0.034	0.046	0.46	0.54
Recovery day 1	ND	ND	ND	ND

---

[a] Total metabolites, 200 ppm:
66.7 ppm carbofuran phenol,
66.7 ppm 3-keto-7-pnenol-carbofuran, and
66.7 ppm 3-hydroxy-7-phenol-carbofuran

[b] No 3-hydroxycarbofuran phenol was detected at a method sensitivity of 0.050 ppm. The analytical method used was microcoulometric gas chromatography with a nitrogen detector, corrected for instrument efficiency and average recovery.

[c] Average of 4 cows.

[d] ND = None detectable.

Source: Shuttleworth (1973).

Table 8. Residues in Tissues of 3 Metabolites of Carbofuran at End of 28-day Feeding Period

Tissue and Feeding level (ppm)[a]	Residue, ppm[b]		
	Carbofuran phenol	3-Keto-7-phenol carbofuran	3-Hydroxy-7-phenol carbofuran
Muscle			
200	ND[c]	ND	ND
200	ND	ND	ND
Liver			
200	ND	ND	ND
200	ND	ND	ND
Fat			
200	ND	ND	ND
200	ND	ND	ND
Kidney			
20	ND	ND	ND
20	ND	ND	ND
60	ND	ND	< 0.10
60	ND	ND	ND
200	0.15	0.27	0.32
200	0.32	0.34	0.40

---

[a] Feeding level of 200 ppm:
66.7 ppm carbofuran phenol,
66.7 ppm 3-keto-7-phenol-carbofuran,
66.7 ppm 3-hydroxy-7-phenol-carbofuran.
Feeding level of 60 ppm:
20 ppm of each of the above.
Feeding level of 20 ppm:
6.7 ppm of each of the above.

[b] Method sensitivity: muscle, liver, and fat, 0.05 ppm; kidney, 0.10 ppm. Analytical method: microcoulometric gas chromatography with a nitrogen detector, corrected for instrument efficiency and average recovery.

[c] ND = None detectable.

Source: Shuttleworth (1973).

Table 9. U.S. Tolerances for Carbofuran

ppm	Crop
10	Alfalfa (fresh) (limited to 5 ppm carbamates)
40	Alfalfa hay (limited to 20 ppm carbamates)
0.1	Bananas
0.05	Cattle (meat, fat, meat by-products) limited to 0.02 ppm carbamates
0.1	Coffee beans
25	Corn fodder and forage (limited to 5 ppm carbamates)
0.2	Corn grain including popcorn (limited to 0.1 ppm carbamates)
0.05	Goats (meat, fat, meat by-products) limited to 0.02 ppm carbamates
0.05	Hogs (meat, fat, meat by-products) limited to 0.02 ppm carbamates
0.05	Horses (meat, fat, meat by-products) limited to 0.02 ppm carbamates
0.1	Milk (limited to 0.02 ppm carbamates)
0.2	Peanuts (limited to 0.1 ppm carbamates)
5	Peanut hulls (limited to 1 ppm carbamates)
1	Peppers (limited to 0.2 ppm carbamates)
2	Potatoes (limited to 1.0 ppm carbamates)
0.2	Rice
1	Rice straw (limited to 0.2 ppm carbamates)
0.05	Sheep (meat, fat, meat by-products) limited to 0.02 ppm carbamates
3	Sorghum fodder and forage (limited to 0.5 ppm carbamates)
0.1	Sorghum grain
0.5	Strawberries (limited to 0.2 ppm carbamates)
0.1	Sugar beets
2	Sugar beet tops (limited to 1 ppm carbamates)
0.1	Sugarcane

Source: Code of Federal Regulations, Title 40, Chapter 1, Part 180, Subpart C, Section 180.254, July 1975, as amended in Federal Register 41(2): 763. January 5, 1976.

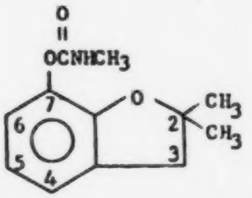
Composition and Formulation

According to the manufacturer (FMC, 1972a), technical carbofuran is 98.8% pure. The other 1.2%, classified as an inert ingredient, is 2,3-dihydro-2,2-dimethyl-7-benzofuranol, an unreacted raw material from the final processing step (see the Synthesis and Production Technology section).

Carbofuran is available in 2 principal formulations from the manufacturer. These are granules, 10, 5, 3, and 2% (designated 10G, 5G, 3G, and 2G), and 4 lb/gal flowable formulation. Two wettable powder formulations (50 and 75%) have been used for crop residue studies, but are not currently available.

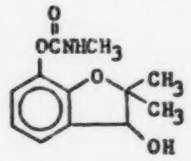
Chemical Properties

Most of the available information on the chemical degradation of carbofuran was obtained by researchers concerned with the metabolism of carbofuran and its degradation in animals and plants. Carbofuran undergoes 3 types of chemical degradation: hydrolysis, oxidation, and photodecomposition. The structures and common names of carbofuran and its principal degradation products are given below.



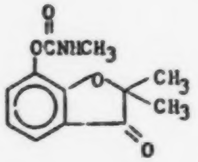
Carbofuran

I



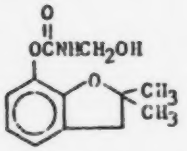
3-Hydroxycarbofuran

II



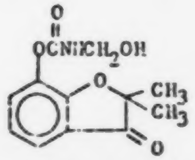
3-Ketocarbofuran

III



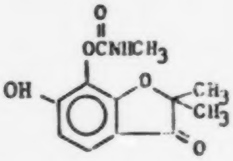
N-Methyl hydroxycarbofuran

IV



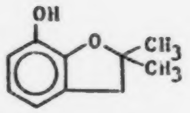
3-keto-N-methyl hydroxycarbofuran

V



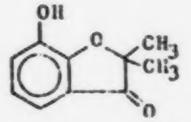
3-Keto-6-hydroxy-carbofuran

VI



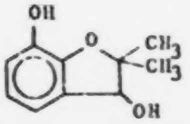
Carbofuran-7-phenol

VII



3-ketocarbofuran-phenol

VIII



3-hydroxy-7-phenol carbofuran

IX

Hydrolysis - Cook (1973) states that carbofuran is stable in neutral or slightly acid solutions, but will hydrolyze under basic or strongly acid conditions. Cleavage occurs at the carbamate linkage.

Metcalf et al. (1968) studied the hydrolysis rate of carbofuran and several of its metabolites in alkaline solution at 37.5°C. The various carbamates were added at 0.1% weight/volume in methanol to phosphate buffer at pH 9.5, and the hydrolysis constants were determined by the rate of formation of the phenolic hydrolysis products which were measured by ultraviolet spectrophotometry. The results are shown below.

	K_{hyd}, min^{-1}	$T_{1/2}$, min
Carbofuran	0.0104	66.9
3-Hydroxycarbofuran	0.0263	26.4
3-Ketocarbofuran	1.715	0.404
N-Methylhydroxycarbofuran	0.130	5.33
3-Keto-N-methylhydroxycarbofuran	>7.0	0.1

Getzin (1973) studied the degradation of carbofuran in soil. Figure 4 shows his results at 4 pH levels in Sultan silt loam. Getzin also studied carbofuran hydrolysis in alkaline (unstated pH) aqueous solution and obtained a half life of 8 days at 25°C. The hydrolysis occurred at the carbamate linkage yielding carbofuran-7-phenol as one product. (Getzin did not report other hydrolysis products, nor did he describe his experimental method.) Getzin concludes that, in alkaline soils, the primary route of degradation is chemical hydrolysis, while in acid or neutral soils slow microbial and chemical degradation occurs.

Caro et al. (1973a) primarily studied dissipation of carbofuran in the soil. They determined the half-life of carbofuran in solution (unspecified concentration) at pH 6.35 and 5.20. The half-life at pH 6.35 was 140 days and at pH 5.20, 1,600 days. The results in soil are discussed in the Fate and Significance in the Environment Section of this report.

Caro et al. (1973a) also estimated the effect of temperature on hydrolysis by utilizing the Arrhenius equation:

$$k = Ae^{-E^*/RT}$$

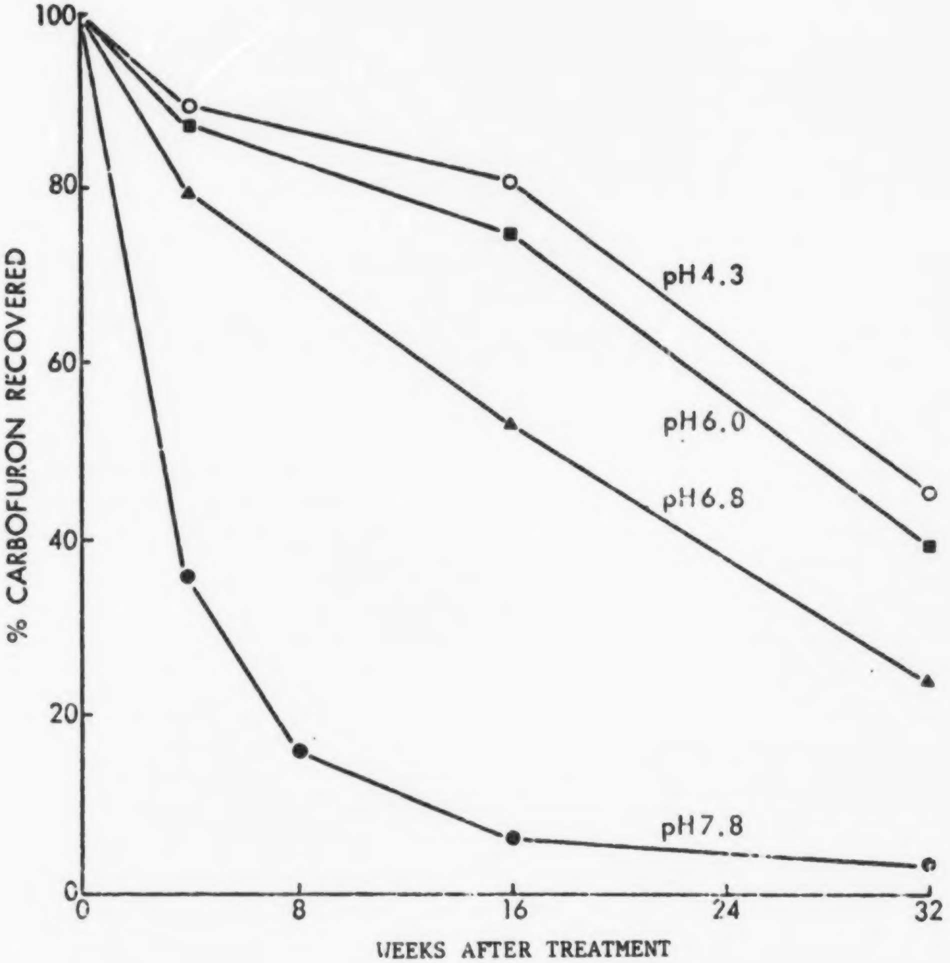


Figure 4. Degradation Curves for Carbofuran in Sultan Silt Loam at 4 pH Levels

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Source: Getzin, L.W. (1973). Persistence and degradation of carbofuran in soil. Environ. Entomol. 2(3):461-467. Reprinted by permission of Entomological Society of America.

Studies were done on the hydrolysis of technical carbofuran, 2 carbofuran formulations, and 3-hydroxycarbofuran, a major metabolite of carbofuran. In the first test, the pH levels were 4, 7, and 9.2; only one analysis was taken after 24 hr. The samples were saturated solutions, buffered in water at 25°C. The results showed little or no hydrolysis at pH 4 and 7, and complete hydrolysis at pH 9.2 (McDonald, 1972).

McDonald then conducted a further test at pH 9.2, which included intermediate measurements. The results are as follows:

Product	Timed interval and rate of hydrolysis (%)			
	0 hr	3 hr	5.5 hr	24 hr
Technical carbofuran	0	39.1	64.4	100
Furadan® 75 WP	0	78.4	79.1	100
Furadan® 10 G	0	20.2	62.4	96.6
3-Hydroxycarbofuran	0	67.2	87.6	100

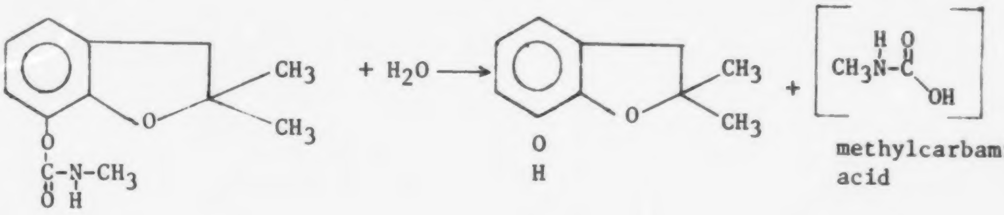
McDonald indicated that the incomplete hydrolysis of the granules was "associated with water release characteristics or solubility of this formulated product in water."

McDonald then studied several pH levels between 7 and 9.2, using the same buffering procedure, but only with technical carbofuran. The results are as follows:

pH	Percent hydrolysis in 24 hr at 25°C
7.0	0
7.6	4.6
8.0	18.2
8.6	31.0
9.2	100

These values may be plotted on a log percent versus time graph and the half-life read from the 50% point (FMC,1972b). A different line (with only the initial and final points) is drawn from each pH value. This method for determining half-life is valid if an assumption of first-order kenetics is correct. This assumption is discussed below. Using this method, the above report gave the following half-lives at 25°C: pH 8.6, 1.9 days; pH 8.0, 3.6 days; pH 7.6, 16.1 days.

The following chemical reaction occurs in hydrolysis under slightly alkaline conditions (pH 5-10).

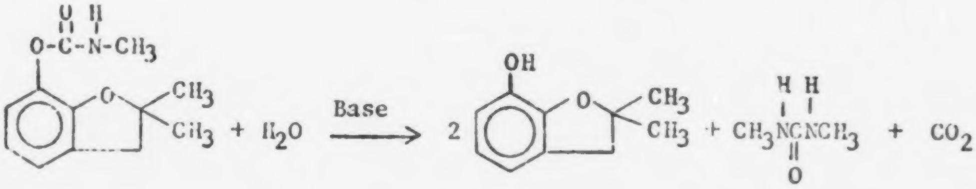


methylcarbamic
acid

$$[CH_3NHCOOH] \longrightarrow CH_3NH_2 + CO_2$$

methylamine

In a strongly alkaline solution such as 20% NaOH, and at temperatures above 100°C, the reaction as given by McDonald (1972), would be of second order with respect to carbofuran.



2,2-Dimethyl-7-
hydroxy-2,3-
dihydrobenzofuran

1,3-Dimethylurea

The rates of hydrolysis under various pH and temperature conditions have been determined. These findings are summarized below (Cook and Robinson, 1972).

pH	Temperature (°C)	Results
5	28	No hydrolysis in 28 days
7	28	Stable for 3 days, 48,4% remaining at 21 days, erratic step pattern
9	28	19.9% remaining after 1 day
9	26	Half-life of 12 hr (0.46 days) (60% remaining after 7 hr)
9	5	Half-life of 1.5 days (53.8% remaining after 1 day (0.7% after 7 days)

Hydroxylation (oxidation) - Metcalf et al. (1968) studied the oxidation of carbofuran in plants, insects, mice, and in a model system. Results are depicted graphically in Figure 5. Major metabolic pathways were: (1) hydroxylation at carbon position number 3, (2) further oxidation to corresponding 3-ketocarbofuran compounds and (3) hydrolysis of carbamate moieties to the corresponding phenols.

Photodecomposition - Metcalf et al. (1968) studied the effects of fluorescent light and sunlight on residues of crystalline carbofuran in Petri dishes. 3-hydroxycarbofuran was detected by thin-layer chromatography (TLC) after 2 days in outdoor sunlight, and also on TLC plates exposed to fluorescent light at 70°F for 1 week. After 2½ weeks, 3 other unidentified compounds were detected in the samples irradiated in sunlight. The authors speculated that one was carbofuran phenol because it did not inhibit cholinesterase. However, none of these compounds were analytically identical. The authors also noted that the 3-ketocarbofuran did not appear.

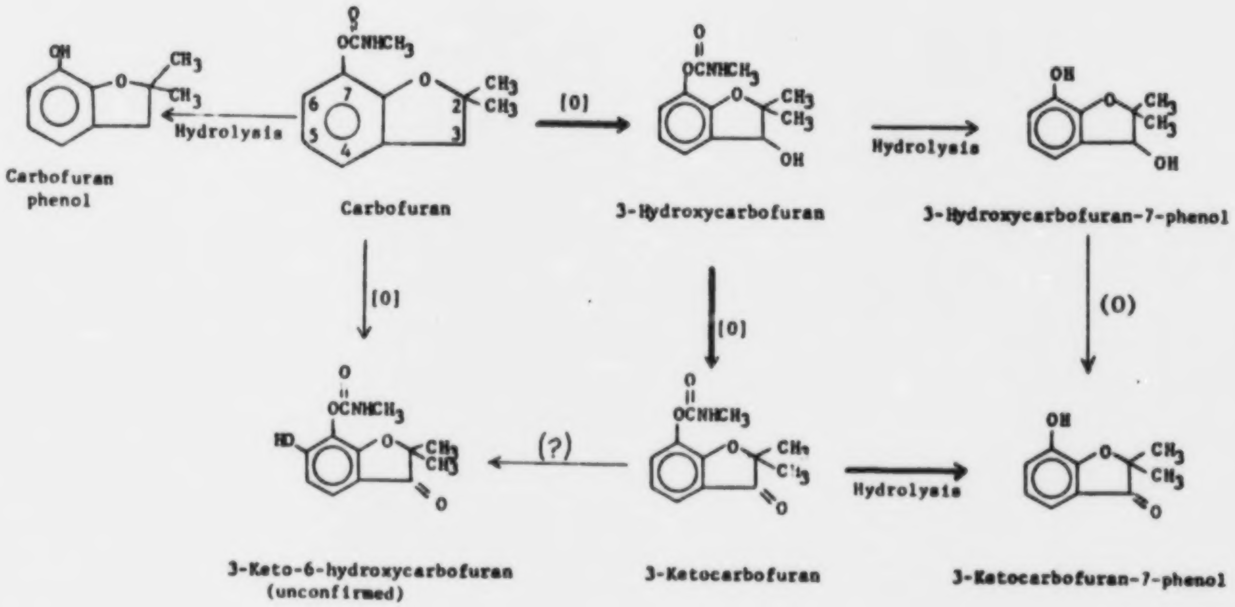


Figure 5. Oxidation and Hydrolysis Routes of Carbofuran

Note: Heavy lines indicate major pathways.

Source: Based on data in Metcalf et al. (1968).

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART B. PHARMACOLOGY AND TOXICOLOGY

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This section is concerned with information on the acute, subacute, and chronic toxicity of carbofuran in laboratory and domestic animals (mice, rats, dogs, rabbits, cattle, sheep, and chickens). A review is given of the characteristic symptoms and pathology of carbofuran poisoning in mammals, in addition to possible antidotes. Studies are discussed concerning the effects of carbofuran on the reproductive cycles of rats and dogs. Oncogenic effects are also considered plus a review of mutagenic, teratogenic and potentiation studies. The section summarizes rather than interprets data reviewed.

Acute, Subacute, and Chronic Toxicity

Acute Oral Toxicity - Rats - A number of acute oral toxicity tests have indicated that the oral LD_{50} for technical carbofuran in the adult rat ranges from 6.4 mg/kg to 14.1 mg/kg (see Table 10). The oral toxicity of a formulation is proportional to the amount of active ingredient present. For example, the oral LD_{50} for the formulation 10G (10% granular) was reported to be 131.2 mg/kg (Schoenig, 1968b). The intraperitoneal LD_{50} of technical grade carbofuran was reported as 1.37 mg/kg (Kohn et al., 1967b).

The acute oral toxicity of different formulations varies with the formulation, but there does not appear to be a sex difference in response. Differences in the sensitivity of the newborn, the weanling, and the adult rat to technical carbofuran are summarized in Table 10.

The acute oral toxicity of carbofuran metabolites was also evaluated. Five metabolites were studied in tests on young albino rats (Sprague-Dawley strain). Selected dosages were given to groups of 4 rats each (2 males and 2 females) by intubation, followed by a 14 day observation period. The results of the tests are summarized in Table 11.

The effect of acute doses of carbofuran on cholinesterase activity was studied in Charles River strain rats. Groups of 25 rats were intubated at dose levels of 0.2, 0.5, 1.0, 3.0, and 10.0 mg/kg. After administration of the pesticide, blood samples were withdrawn from the orbital sinuses of the animals. Brain cholinesterase was determined in groups of 5 animals at 1, 2, 4, 6, and 24 hr. The results for the various dose levels were as follows: At 0.2 mg/kg there was no effect on plasma, red blood cell (RBC) or brain cholinesterase at 1, 2, 4, 6, or 24 hr. At 0.5 mg/kg, the only effect seen was a 36% depression of brain cholinsesterase at 6 hr. There was no effect on brain or blood cholinesterase at other intervals. At 1.0 mg/kg, a 49% depression of brain cholinesterase was noted at 6 hr, but no depression at 1, 2, 4, or 24 hr. Plasma cholinesterase was depressed at 1, 2, 4, and 6 hr, but returned to normal at 24 hr. No effect on RBC cholinesterase was observed. At 3.0 mg/kg, there was a depression of plasma and brain cholinesterase up to 6 hr which returned to normal at 24 hr. No effect on RBC activity was noted at 1, 2, 4, 6, or 24 hr. At 10.0 mg/kg, there was a significant mean depression of brain cholinesterase levels at 1, 2, 4, and 6 or 24 hr. Marginal effects on RBC activity were observed at 2, 4, and 24 hr (Kretchmer, 1972).

Table 10. Summary of Acute Toxicity Data for Rats

Animal	Formulation	Administration	Toxicity	Reference
Rat a/	Tech. (PG)*	Oral	LD$_{50}$ = 7.1 mg/kg (± 0.7)	Palazzolo (1963a)
Rat a/	Tech. (PG)	Oral	LD$_{50}$ = 6.4 mg/kg	Palazzolo (1963a)
Rat b/	Tech. (PG, CO)**	Oral	LD$_{50}$ = 14.1 mg/kg (8.91-22.4)	Powers (1964)
Rat c/	Tech. (CO)	Oral	LD$_{50}$ = 11.9 mg/kg (± 2.5)	Kohn et al. (1967a)
Rat (M) a/	Tech. (CO)	Oral	LD$_{50}$ = 11.34 mg/kg (± 1.15)	Schoenig (1967f)
Rat (F) a/	Tech. (CO)	Oral	LD$_{50}$ = 11.34 mg/kg (± 2.16)	Schoenig (1967f)
Rat (M) a/	Tech. (CO)	Oral	LD$_{50}$ = 8.2 mg/kg	Schoenig (1966)
Rat (newborn) a/	Tech. (CO)	Oral	LD$_{50}$ = 1.65 mg/kg (± 0.24)	Schoenig (1967f)
Rat (weanling) a/	Tech. (CO)	Oral	LD$_{50}$ = 3.36 mg/kg (± 0.64)	Schoenig (1967f)
Rat a/	10 G	Oral	LD$_{50}$ = 131.2 mg/kg (± 13.3)	Schoenig (1968b)
Rat a/	Tech. (PG)	Oral	LD$_{1}$ = 5.3 mg/kg (-)	Palazzolo (1963a)
Rat a/	Tech. (PG)	Oral	LD$_{99}$ = 9.5 mg/kg (-)	Palazzolo (1963a)
Rat c/	Tech. (PG)	Intraperitoneal	LD$_{50}$ = 1.37 mg/kg (± 0.17 mg)	Kohn et al. (1967b)
Rat c/	Tech. (PG)	Intraperitoneal	LD$_{1}$ = 1.05 mg/kg	Kohn et al. (1967b)
Rat c/	Tech. (PG)	Intraperitoneal	LD$_{99}$ = 1.80 mg/kg	Kohn et al. (1967b)

* PG = Propylene glycol carrier.
** CO = Corn oil carrier.

a/ Sprague-Dawley strain.
b/ Unspecified strain.
c/ Simonson Laboratory strain.

Table 11. Acute Oral Toxicity of Carbofuran Metabolites

Metabolite	LD_{50}	Reference
2,3-Dihydro-2,2-dimethyl-7-hydroxybenzofuran	2.2 ± 0.5 g/kg[a] 1.8 ± 0.4 g/kg[b] 1.8 ± 0.3 g/kg[c]	(Schoenig, 1967b)
2,3-Dihydro-7-hydroxy-2,2-dimethyl-3-oxobenzofuran	295.1 ± 29.96 mg/kg[d]	(Schoenig, 1967c)
2,2-Dimethyl-3,7-dihydroxy-2,3-dihydrobenzofuran	1,350 ± 158.4 mg/kg[d]	(Schoenig, 1967d)
3-Hydroxycarbofuran	17.9 ± 4.3 mg/kg[e]	(Schoenig, 1967e)
3-Ketocarbofuran	69.0 ± 14.7 mg/kg[f]	(Schoenig, 1967e)

a/ Undiluted.
b/ 25% (w/v) corn oil solution.
c/ 75% (w/v) propylene glycol solution.
d/ 5% (w/v) corn oil suspension.
e/ 0.1% (w/v) suspension in corn oil.
f/ 1% (w/v) suspension in corn oil.

Acute Oral Toxicity - Dogs - The results of oral toxicity tests indicated that dogs were somewhat more resistant than rats to the action of carbofuran. The LD_{50} for dogs is reported to be 18.85 mg/kg. However, acute inhalation tests indicated that the dog was equally susceptible by the respiratory route (see Table 12).

During an acute toxicity study with beagle dogs, the inhibition of blood cholinesterase by technical carbofuran was also investigated. The reduction of cholinesterase activity for plasma and erythrocytes with time and dose is shown in Tables 13 and 14 (Baran, 1967a). The lowest level of cholinesterase activity appeared following the first hr of administration. Signs of recovery were observed at 24 hr (Baran, 1967a).

Table 12. Summary of Acute Toxicity Data for Animals Other Than Rats

Animal	Formulation	Administration	Toxicity	Reference
Dog[a]	Tech. (GC)*	Oral	LD_{50} = 18.85 mg/kg (± 1.02)	**Baran (1967a)**
Dog[a]	Tech.	Oral	LD_1 = 16.46 mg/kg (-)	**Baran (1967a)**
Dog[a]	Tech.	Oral	LD_{99} = 21.55 mg/kg (-)	**Baran (1967a)**
Rabbit[b]	Tech.	Dermal	LD_{50} = 14.7 mg/kg	Palazzolo (1963a)
Rabbit[b]	10 G	Dermal	LD_{50} = 10.2 g/kg	Schoenig (1967a)
Rabbit[b]	Furadan® 4 (flowable, paste)	Dermal	LD_{50} = 6.8 g/kg (± 0.8)	Schoenig (1968a)
Chicken[d]	Tech.	Oral	LD_{50} = 25.0 mg/kg (12.5-50)	**Palazzolo (1966)**
Chicken[d]	Tech.	Oral	LD_{50} = 38.9 mg/kg (-)	**Jackson (1967)**
Mouse	Tech.	Oral	LD_{50} = 2 mg/kg	**Fahmy et al. (1970)**

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* GC = Gelatin capsule.

[a] Beagle.
[b] New Zealand albino strain.
[c] English strain.
[d] White leghorn strain.

Table 13. Changes in Plasma Cholinesterace Activity in Dogs After Dosing With Carbofuran

Dog		Dose (mg/kg)	Cholinesterase activity[a/] Time after dose (hr) 0	1/2	1	2	24
1	(male)	15.38	0.499	0.455	0.364	0.510	0.444
2	(female)	15.38	0.471	0.372	0.333	0.305	0.446
3	(male)	23.07	0.516	0.291	0.184	-[b/]	-
4	(female)	23.07	0.470	0.297	0.300	0.401	0.398

a/ Acetic acid (µm/min/ml) of plasma.
b/ Dog died.
Source: Baran (1967a).

Table 14. Changes in Erythrocyte Cholinesterase Activity in Dogs Dosed With Carbofuran

Dog		Dose (mg/kg)	Cholinesterase activity[a/] Time after dose (hr) 0	1/2	1	2	24
1	(male)	15.38	0.328	0.259	0.243	0.274	0.315
2	(female)	15.38	0.336	0.312	0.277	0.243	0.296
3	(male)	23.07	0.273	0.263	0.171	-[b/]	-
4	(female)	23.07	0.361	0.132	0.311	0.294	0.321

a/ Acetic acid (µm/min/ml) erythrocytes.
b/ Dog died.
Source: Baran (1967a).

Acute Dermal Toxicity - Rabbits - Furadan (4 lb/gal) was applied as an aqueous slurry to the shaved skin of rabbits. Animals were wrapped and a plastic collar was used to prevent migration of the test material during the 24 hr exposure. All animals that died, as well as survivors, were necropsied (Schoenig, 1967a).

Animals that received doses of 4.6, 6.8, and 10.2 g/kg showed hypoactivity and muscular weakness 1 to 6 hr posttreatment. Reactions continued 1 to 2 days in survivors. Salivation, tremors, fibrillary action and miosis were noted at 6.8 and 10.2 g/kg, 1 to 6 hr after treatment and continued 6 to 18 hr.

Skin reactions were characterized by pale, red, definable erythema in all dose groups at termination of the 24 hr contact period. At 7 and 14 days following treatment, only dryness and desquamation of skin were noted at the application site. No significant pathological alterations were noted in any animal at necropsy. The acute dermal LD_{50} was calculated to be 6.8 g/kg (± 0.8) (Schoenig, 1968b).

The acute dermal LD_{50} of technical carbofuran in an organic solvent (Dowanol DPM) for rabbits was determined to be 14.7 mg/kg; however, the acute dermal LD_{50} of the technical carbofuran in water was greater than 10.2 g/kg (FMC, 1963 and 1969).

Acute Oral Toxicity - Mice - The acute oral LD_{50} for technical carbofuran administered to Swiss mice was determined to be 2 mg/kg body weight (Fahmy et al., 1970).

Acute Oral Toxicity - Chickens - The acute oral toxicity for chickens was reported to range from LD_{50} 25.0 to LD_{50} 38.9 mg/kg. This data indicates that chickens possess more resistance to carbofuran than any other animal for which data is available (Palazzolo, 1966 and Jackson, 1967). The LD_{50}'s reported for domestic chicken also indicate that this bird is more resistant to the acute toxic effects of carbofuran than wild birds (see section on Effects on Wildlife).

Acute Oral and Topical Toxicity - Cattle - In a metabolism study, administration of a single 0.52 mg/kg dose of carbofuran to 1 cow resulted in marked nervousness of the animal for about 3 hr, but no other signs of poisoning appeared. Another dose of 1.0 mg/kg caused salivation, tearing, hyperactivity, and diarrhea within 50 min after dosing. The signs of toxicity were most severe after 2 hr but subsided to an apparent normal condition in 4 hr (Ivie and Dorough, 1968).

In another study, a 635 kg Holstein cow was given a single 5 g (7.9 mg/kg) oral dose of carbofuran. The animal exhibited extreme signs of distress within 30 min. The signs of poisoning were very rapid breathing and muscular twitching followed by convulsions. One hr after administration of carbofuran, the animal was treated with atropine sulfate, and recovery appeared complete within 12 hr (Miles et al., 1971).

The effects of oral dosage and topical application of carbofuran to 1- to 2-week-old calves and older cattle was studied. The compound was administered orally as a 75% wettable powder or as 96.7% technical grade carbofuran, in gelatin capsules, 1 hr after feeding.

Intoxication in the 1- to 2-week-old calves resulted from oral doses of 0.25 mg/kg or greater. At 1 mg/kg, 1 animal died even though it was treated with atropine sulfate. Necropsy findings (1 mg/kg) were congestion of the lungs and reddening of the visceral mucosa. In older cattle, the highest oral dose of carbofuran (1.0 mg/kg) resulted in only mild signs of toxicosis which did not necessitate administration of atropine sulfate.

For topical application, 4 liters of an 0.01, 0.05, or 0.19% spray were administered. Animals receiving topical applications greater than 0.05% carbofuran (4 liters of emulsion) showed mild signs of toxicity. Signs of toxicity occurred within 1 hr after treatment. Animals treated topically with 0.1% emulsion required atropine sulfate treatment to prevent death.

Two yr-old heifers receiving 0.05% topical applications showed signs of toxicity but did not require atropine sulfate treatment. At 0.1%, yearlings exhibited increased salivation, muscular tremors and prostration. Washing away the residual and atropine sulfate treatment was required to save the animals. Animals showing indication of toxicosis generally had depressed blood cholinesterase levels (Palmer and Schlinke, 1973).

Acute Oral Toxicity - Sheep - Carbofuran was administered orally to yearling crossbred sheep as single 1.0, 5.0, 10.0, and 25.0 mg/kg doses in gelatin capsules. Doses higher than 2.5 mg/kg body weight resulted in severe toxicosis requiring atropine treatment to save the animals. One animal receiving a 10.0 mg/kg dose died within 2 hr in spite of atropine treatment. The severity of toxicosis was generally indicated by reduced blood cholinesterase levels. The animal that died after treatment with 10 mg/kg carbofuran exhibited pulmonary edema and congestion of internal organs (Palmer and Schlinke, 1973).

Subacute Oral Toxicity - Rats - The subacute toxicity of technical carbofuran for Sprague-Dawley rats was determined over a period of 90 days (Kohn, 1965). The test groups established and the feeding schedule for each group are shown below. Ten males and 10 females were used for each test group and for the controls. Diets were fed *ad libitum*:

Carbofuran (ppm) fed for indicated days

	0-21	22-35	36-49	50-90
Controls	-	-	-	-
Test group				
I	0.1	0.4	1.6	1.6
II	0.4	1.6	6.4	6.4
III	2.0	8.0	32.0	32.0
IV	10.0	40.0	160.0	160.0
V	25.0	100.0	400.0	1,600.0

After 90 days all animals were sacrificed. Standard gross and microscopic pathological examinations were conducted on several organs including the liver, kidney, spleen, gonads, heart, and brain.

Some effects on growth were noted in both males and females. Lowered weight gains were recorded for both sexes in Treatment Groups IV and V. It was suggested that reduced palatability in the higher treatment groups may have contributed to the reduced weight gains (192 g weight gain for controls, 171 g for Group IV females and 133 g for Group V females). There were no differences between controls and treated animals in hematology, urinalysis, behavioral effects, gross pathology, microscopic pathology, and in selected organ weights. No deaths were recorded throughout the study (Kohn, 1965).

In another test, groups of Charles River albino rats (15 males and 15 females per group) were fed carbofuran for 90 days at dose rates of 0, 300, 1,000, and 3,000 ppm. During the feeding period, weight gains were determined at weekly intervals and food consumption was carefully monitored for 5 animals of each sex per test group. Mortality and abnormal reactions were recorded daily Blood and urine samples were collected from 10 rats of both sexes for the control and 3,000 ppm test groups after 45 and 84 days of feeding. Hematology, blood chemistry, and urinalysis were monitored.

All animals were sacrificed at the end of 90 days of feeding and each was subjected to necropsy. Weights of livers, kidneys, spleens, gonads, hearts, and brains were recorded. Microscopic examination was carried out on tissues from 10 rats of each sex for the control and the 3,000-ppm test group.

An examination of the results of all tests indicated no significant difference between the control and the test group for any parameter compared (Reyna, 1972). Charles River strain albino rats were dosed at 0.1, 0.3, 1.0, and 3.0 mg/kg/day for 16 weeks (propylene glycol solutions, intubated) and the effect of treatment on cholinesterase activity was then determined after 1, 3, 6, and 13 weeks. After 13 weeks, treatment was reported to have caused little reduction of cholinesterase activity at the highest concentration (3.0 mg/kg) used.

Some of the 13-week values obtained in this study are shown below:

Cholinesterase activity[a]

		Plasma	Erythrocyte	Brain
Controls -	Male	0.263	0.513	4.277
	Female	0.390	0.383	4.826
Test -	Male	0.275	0.530	5.196
	Female	0.492	0.491	5.080

[a] Acetic acid (μm/min/ml) of plasma or erythrocytes and μm/min/g for brain.

Source: Wolf (1966a).

The effect of time of sampling on cholinesterase activity was shown by Wolf in a subacute study using female Charles River rats. After dosing at 3.0 mg/kg/day for 3 weeks (technical carbofuran), blood samples were drawn at intervals from 0 time (after dosing) to 60 min. The following results suggest that a depression of cholinesterase acitivity is observed if sampling is done a short time following dosing:

Effect of time of sampling on cholinesterase activity

Time of sampling: after dosing	Cholinesterase activity[a/] Erythrocyte	Plasma
0	0.482	0.323
15 min	0.396	0.251
30 min	0.361	0.245
45 min	0.370	0.205
60 min	0.329	0.1522

a/ Acetic acid (μm/min/ml).

Source: Wolf (1966a).

A 28-day cholinesterase study was performed using female Charles River rats (Plank, 1972). A group of 40 rats was administered daily doses of 1.0 mg/kg carbofuran in corn oil by gavage. A control group of 10 animals was given daily doses of corn oil by gavage. At 14 and 28 days, 5 test animals were sacrificed 1, 2, 6, and 24 hr following carbofuran administration. Five control animals were also sacrificed at 14 and 28 days. Plasma, RBC and brain cholinesterase activity were determined for each animal sacrificed.

In the 14- to 28-day test, only slight depression (less than 15%) of plasma or RBC cholinesterase was observed 1 to 6 hr after dosing. However, because a single 1 mg/kg dose resulted in 30% depression in 1 to 6 hr in other animals, the investigator concluded that daily exposure resulted in some adaptation during the 14- or 28-day exposure periods.

Brain cholinesterase was significantly depressed after 2 and 6 hr at the 14- and 28-day exposure periods. The cholinesterase level returned to normal within 24 hr. The results suggest there is no adaptive mechanism for brain cholinesterase depression by carbofuran (Plank, 1972).

Ninety-day subacute tests for oral toxicity were conducted using 3-hydroxycarbofuran at dietary levels of 10, 30, and 100 ppm (Plank, 1969) and 2,3-dihydro-2,2-dimethyl-7-hydroxybenzofuran at 300, 1,000, and 3,000 ppm (Reyna, 1972). Charles River strain rats were used as test animals.

At 100 ppm 3-hydroxycarbofuran, no differences in behavior, mortality, hematologic, biochemical or urologic tests were observed between the treated animals and the controls. Data from gross pathological examinations indicated that differences due to treatment could not be identified.

Differences between untreated rats and those fed 2,3-dihydro-2,2-dimethyl-7-hydroxybenzofuran at 3,000 ppm were not observed for body weight, food consumption, mortality, behavioral reactions, hematological tests, blood chemistry, urine constituents, or gross pathology. Erythrocyte cholinesterase activity of treated animals (3,000 ppm, 90 days) was not inhibited as a result of feeding the metabolite.

Subacute Oral Toxicity - Dogs - In an effort to establish a maximum dose level that would have no effect on plasma or erythrocyte cholinesterase, a study was conducted for 92 days by treating beagle dogs with technical carbofuran. Both male and female pure-bred beagles were used; 3 males and 3 females at each of 5 dose levels. When cholinesterase activity was determined 20 hr after dosing, no significant differences were reported between controls and animals treated at the highest concentration, 5 mg/kg/day. Although differences in cholinesterase activity were not noted, the dogs treated at 5 mg/kg/day exhibited frequent coughing and gagging, occasional salivation, muscular tremors and emesis (Baran, 1966).

Subacute Oral Toxicity - Rabbits - A study was conducted to assess possible hazards to rabbits feeding on alfalfa treated with carbofuran. The dietary levels were 70, 210, and 700 ppm. Seventy ppm was considered the average 0 day deposition on 8-in alfalfa when applied at the rate of 1.0 lb/acre. These 3 levels were fed to groups (3 males and 3 females per group) of albino rabbits for 14 days.

No deaths or untoward behavioral reactions were noted. Slight adverse effects on body weights were noted among animals in all groups; however, 5 of 6 animals in the 700 ppm group lost weight while only 1 or 2 animals in other groups lost weight. The weight losses may have been due at least in part to a slight reduction in food intake (Mastri, 1967).

Subacute Oral Toxicity - Chickens - The effects of 3 phenolic metabolites of carbofuran were studied in chickens (Hybrid laying hens). Groups of 10 birds each were fed 3 levels of mixtures of the metabolites 3-hydroxycarbofuran phenol, 3-ketocarbofuran phenol, and carbofuran phenol as indicated below:

Group	No. of animals	Dietary level--carbofuran (ppm)	Dietary level--metabolites (ppm)
1	10	0	0
2	10	20	6.67
3	10	60	20
4	10	200	66.7

Source: Reno (1973b).

The diets were fed for 28 days to determine the levels of metabolites which would occur in eggs and body tissue and to determine the rate at which the metabolites clear the system upon withdrawal from the diet.

After the 28-day feeding period, 5 birds from each of the 4 groups were sacrificed. Following a 15-day recovery period, the remaining birds were sacrificed.

Appearance, behavior, body weights, food consumption, and egg production were observed throughout the feeding and recovery periods. At necropsy, liver, gizzard, skin, fat, heart, muscle, and kidney were taken for analysis of residues.

There were no significant differences observed in appearance, behavior, food consumption, and egg production between the control group and the test groups. No gross pathological alterations or tissue changes were observed at the time of sacrifice. No results were reported for the analysis of tissues and eggs (Reno, 1973b).

Subacute Oral Toxicity - Cattle - The effects of 3 metabolites of carbofuran were also studied in the lactating Holstein dairy cow, using groups of 10 animals each. They were fed the same levels and dosages of phenolic metabolite mixtures as reported in the chronic study on chickens (Reno, 1973b).

The diets were fed to the cows for 28 days to determine the levels of metabolites which would occur in milk and tissues and to determine the rate at which the metabolites clear the system upon withdrawal from the diet.

After being fed the metabolite for 28 days, 2 animals from each of the 4 groups were sacrificed. Following a 15-day recovery period on the basal diet without metabolites, the remaining animals were sacrificed.

Body weights and food consumption were recorded for each animal throughout the test period and milk samples were taken for residue analysis. At sacrifice, gross necropsies were performed and samples of muscle, fat, liver, and kidneys were taken for residue analysis.

Except for 2 injuries and a minor respiratory infection, no untoward effects were observed in the animals during the test. All but 2 of the cattle receiving metabolites showed an unexpected decrease in body weight during feeding. However, these animals began to gain weight during the recovery period. No gross tissue changes were observed in any of the animals sacrificed (Reno, 1973a).

Chronic Oral Toxicity - Rats - Long-term chronic toxicity tests (2 yr) with Charles River albino rats treated at dietary levels of 1, 10, and 100 ppm did not result in any mortality in the treated groups that could be attributed to carbofuran consumption (50% of the animals died).

Both males and females in the 10 ppm test group exhibited a weight depression, but this lowered gain was confirmed statistically ($P<0.05$) only in males.

Throughout the study no behavioral abnormalities were observed to have resulted from treatment.

Blood studies were conducted at the end of the treatment period (2 yr), but no difference between controls and the highest treatment level could be detected for values of hemoglobin concentrations, hematocrits, erythrocyte counts, leucocyte counts and differentials.

Blood chemistry tests were done for blood urea nitrogen (BUN), serum alkaline phosphatase activity (SAP), and serum glutamic pyruvic transaminase (SGPT). Differences could not be detected between the controls and treated animals.

Gross pathological examinations were conducted at 12 months and at 2 yr. The only abnormality noted was the spleen weight in males treated at 100 ppm for 1 yr (5 males and 5 females from the controls and the 100-ppm group were examined). The difference between the control values and the 100-ppm group, however, was not found to be statistically significant. The author reported that the finding may be important because of the observed weight loss which occurred in these males.

All animals that survived for 2 yr were sacrificed and gross and microscopic pathological examinations were conducted.

No differences in gross pathology could be detected between the controls and the treated rats. Histopathological examination confirmed the absence of differences between treated groups and controls.

Absolute organ weights of liver, kidney, spleen, gonads, heart, and brain and organ-to-body or organ-to-brain weight ratios did not reveal any consistent differences between the control animals and those fed carbofuran (Wolf, 1967b).

In another 2 yr chronic study, dietary levels of technical carbofuran of 25 and 50 ppm were fed to Charles River albino rats (Plank, 1968). Seventy animals (35 males and 35 females) were included in each test group. A total of 77% of the animals died during the test, but since mortality was randomly scattered throughout controls and treatment, the deaths were not considered to have been related to treatment.

A reduction in food consumption was noted only in males at the 50-ppm level during the first 9 months of the study. Females fed 50 ppm, and both males and females fed 25 ppm, consumed feed at intakes comparable to untreated controls.

At the dietary level of 50 ppm, males gained less than controls for the first 12 months; thereafter, the gain was similar.

No differences were noted in gross pathology between untreated controls and carbofuran-fed animals (Plank, 1968).

Wolf reported no significant difference between control and test groups with regard to weight gain, food consumption or behavioral effects. Gross pathological examination and examination of tissues collected at necropsy revealed no significant differences between the control and test groups at the end of the 2-yr feeding study (Wolf, 1968).

Chronic Oral Toxicity - Dogs - Pure-bred beagle dogs were fed carbofuran for 2 yr according to the schedule shown below.

Test group	Dietary level (ppm)	Days fed
I	1	1-267
	2	268-737
II	10	1-267
	20	268-737
III	50	1-142
	100	143-730
IV	100	1-267
	200	268-737
V	100	1-14
	200	15-267
	400	268-737

At the end of the 2-yr period, comparisons of treated and control groups were made for food consumption, hematology, blood chemistry, liver function, urine analyses, organ weights, and pathology (gross and microscopic). No significant differences were observed between treated and control groups.

Abnormal behavioral reactions were not observed in dogs at 1, 2, 10, 20, and 50 ppm. At 100 ppm (Groups IV and V), minimal coughing and gagging were observed. At 200 to 400 ppm (Groups IV and V), dogs showed a slight coughing and gagging. Slight salivation, emesis, muscular tremors and weakness in the hindquarters were observed in dogs of Group IV (200 ppm) at 500 to 737 days, and in dogs of Group V (200 to 400 ppm) at days 15 to 737. Fatalities occurred in the Test Group V animals at 400 ppm (Baran, 1967b and 1967c).

Reproduction Studies

Effects on Reproduction - Rats - A 3-generation reproductive study was conducted with weanling rats (Charles River - Sprague-Dawley derived) which were fed diets containing 1, 10, or 100 ppm technical carbofuran (Kennedy, 1967b). Each of the 3 test groups and the control group consisted of 8 males and 16 females which were parents for the first generation of the study. Parental stock and progeny were produced by following the scheme outlined in Figure 6. Animals from each generation were maintained on their respective test diets until sacrifice.

Eight males and 16 females from the second litters of each group were randomly selected at weaning for use as parental animals for the succeeding generation. Mating was conducted when the animals were 100 days old. At 100 ppm, a weight depression was noted in the males (10 to 18% below untreated controls). All deaths that occurred were reported to be due to respiratory infection and not to treatment with carbofuran.

Mating and fertility indices of the 100 ppm test animals were similar to those of untreated controls. In all 3 generations most of the 100 ppm females delivering apparently normal pups lost their entire litters prior to weaning at 21 days.

A greater incidence of stillbirths was observed for all 3 generations in the 100 ppm test group than in the controls or in any of the other treatment groups (Kennedy, 1967b).

A 1-generation reproductive study was conducted with Charles River rats at dietary levels of 0 and 50 ppm carbofuran (Kennedy, 1967a). The weanling body weights in the F_{1a} and F_{1b} test groups were lower than the corresponding control groups. The 5-day survival indices for the treated F_{1a} and F_{1b} groups were also lower (44.7 for F_{1a} and 30.4 for F_{1b}) than the same indices for the controls (96.6 for F_{1a} and 76.8 for F_{1b}). These results appear to parallel the above studies performed at 100 ppm by Kennedy (1967a).

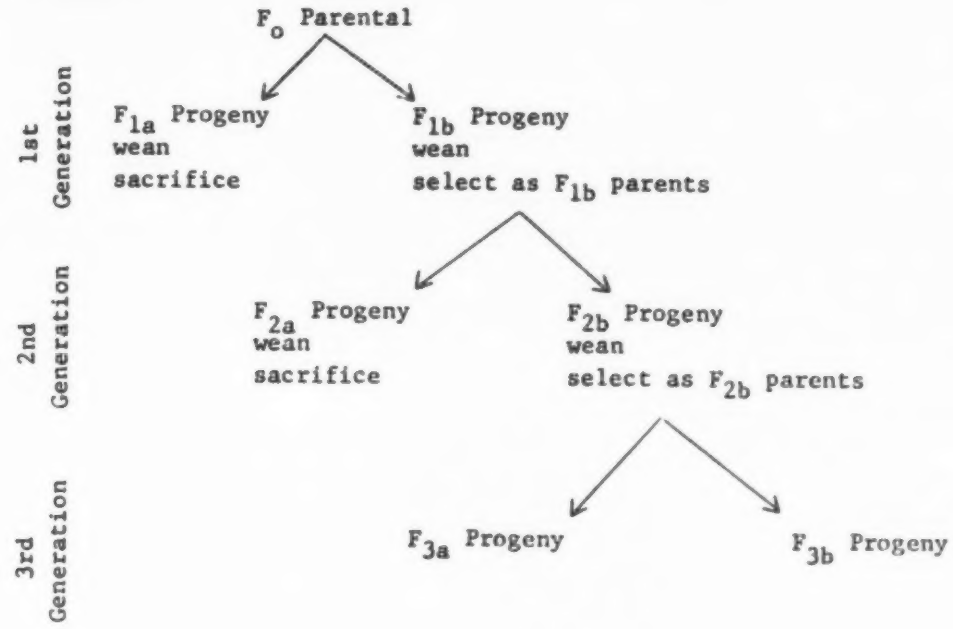


Figure 6. Scheme for Producing Parental and Progeny Stock for a 3-Generation Study (Rats)

Source: Adapted from Kennedy (1967b).

A second-generation study on albino Charles River rats used 2 groups of 24 animals each (8 males and 16 females). One group was given 30 ppm carbofuran in the diet while the other group was maintained on a diet containing no carbofuran.

No significant differences in body weights and no untoward behavioral reactions were noted in the F_1 parental animals. No gross pathological alterations or histopathological differences were observed in test or control F_1 animals.

Mating indices and incidences of pregnancy and parturition were significantly lower in the test than in the control groups. The first litter lactation index was also lower for the test group. The number of pups born and the number of pups viable at various periods of lactation were lower in both litters (F_{2a} or F_{2b}) for the test groups as compared to controls. In the first litters only the 5-day survival index was lower for the test groups; however, all survival indices were lower for second litters of the test group.

The only significant differences in weights of weanlings were observed in second litter females which had lower average body weights than the controls (Arnold, 1968a).

Feeding carbofuran at 30 ppm generally appeared to have affected the mating of parental animals and to have had a subsequent effect on the progeny. The survival indices for all 3 generations are shown in Table 16 (Arnold, 1968b).

Metabolite Study - The compound 3-ketocarbofuran phenol, a metabolite of carbofuran, was fed to Charles River albino rats at dietary levels of 10 and 50 ppm. The animals were mated when they were 100 days old (79 days on test). After 32 weeks, when the F_{1b} litters were weaned, the F_0 parents were sacrificed and subjected to gross pathological examinations.

The results of this study indicated that the metabolite had no effect on the ability of the animals to mate or on the females' ability to conceive and carry the young. There were no differences between the treated and the controls in (a) the number of pups delivered; (b) the number of stillborn; (c) viable pups at birth; (d) number of pups weaned; (e) survival of pups; (f) weanling body weights; (g) physical reactions; or (h) physical appearances of pups.

Histopathological examinations indicated that there were no differences between untreated controls and treated animals (Arnold, 1969).

Effects on Reproduction - Dogs - A reproduction study was carried out with dogs fed dietary levels of 20 and 50 ppm carbofuran for 20 months. One male and 4 females were used per group. One control and 2 test groups of 6-month-old virgin females were fed *ad libitum* for the duration of the study. The

Table 15. Survival Indices for a 3-Generation Study on Rats (30 ppm Carbofuran)

		Live birth index[a]	24-Hr survival index[b]	5-Day survival index[c]
Controls:	F_{1a}	93.5	97.9	95.1
	$F1_b$	98.9	98.3	79.1
	F_2a	92.5	92.6	89.0
	F_{2b}	100.0	97.5	82.5
	F_{3a}	79.3	82.6	73.0
	F_{3b}	92.4	84.5	47.4
30 ppm test:	F_{1a}	90.5	90.3	82.1
	F_{1b}	94.7	96.0	80.7
	F_{2a}	90.6	88.5	70.1
	F_{2b}	85.7	66.7	55.6
	F_{3a}	85.0	100.0	94.1
	F_{3b}	84.6	100.0	36.4

[a] Live birth index: $\frac{\text{viable pups}}{\text{total pups}} \times 100$

[b] 24-Hr survival index: $\frac{\text{pups viable on lactation day 1}}{\text{viable pups}} \times 100.$

[c] 5-Day survival index: $\frac{\text{pups viable on lactation day 5}}{\text{viable pups born}} \times 100.$

Source: Adapted from Arnold (1967, 1968a, 1968b).

study was terminated after litters of 3 or 4 females per group were 4 weeks old. At 1 week, X-rays were taken of each pup to determine any adverse effects on skeletal development. At 4 weeks, 1 male and 1 female from each litter were sacrificed and subjected to complete pathological examination.

The results showed no adverse effects on parental animals with respect to mortality, general reactions, body weight, food consumption, estrus cycles, mating performance, parturition and lactation. No adverse effects were observed in the progeny of control or test animals with respect to litter size, survival indices, general reactions, body weights, ability to nurse, or skeletal abnormalities and gross pathological findings (Stephens, 1970).

Three pregnant female beagle dogs were fed carbofuran in the diet at 20 ppm during the last half of the gestation period and continuing through lactation. Initially, the dietary level was 5 ppm but it was increased every 5 days by 5 ppm until 20 ppm was reached.

The females did not exhibit any physical signs of intoxication during the test period. All the pups born of these test animals appeared normal and maintained normal growth patterns (Carlson, 1968).

Oncogenic Effects

Oncogenic Effects - Mice - The carcinogenicity of technical carbofuran to Charles River, random-bred mice was considered in a study by Reyna (1973). The mice were divided into 4 groups of 100 animals (50 males and 50 females). One group was held as untreated controls and 2 of the remaining 3 groups were given carbofuran in the diet at 30 and 100 ppm. The last group was a positive control and was given urethane at 600 ppm. The mice were fed on their respective diets for 18 months.

Each animal was examined weekly for signs of tumor formation and complete gross pathological examinations were conducted on all postmortem animals and on all animals surviving the treatment.

Tumors were observed in test animals, but they were not different in number nor in their latent periods from those observed in untreated animals. Treatment with urethane resulted in an increase in tumor incidence. A summary of tumor incidence is given in Table 16 (Reyna, 1973).

Oncogenic Effects - Rats - Rats fed 100 ppm dietary carbofuran in a chronic toxicity study were evaluated after 2 yr for incidence of tumors. The results indicated that the incidence of tumors in treated animals was not related to treatment with carbofuran.

Dietary dose (ppm)	Tumor incidence (%)
0	24.2
1	12.5
10	15.6
100	8.8

Source: Wolf (1967a and 1967b).

The tumors found were primarily chromophobe adenomas of the pituitary and mammary adenofibromas (Wolf 1967a and 1967b).

Treated survivors fed up to 50 ppm carbofuran for 2 yr had the same incidence of tumors as untreated controls (Plank, 1968).

Table 16. Summary of Tumor Incidence During an 18-Month Carcinogenic Study With Swiss White Mice

Groups	Control	Positive control	Carbofuran 30 ppm	Carbofuran 100 ppm
Number submitted for histopathologic examination[a]	57	25	31	39
Number with tumors	6	19	5	8
Percent of total examined with tumors	10.5	76.0	16.1	20.5
Type of tumor		Number of tumors		
Alveologenic adenoma	4	16	4	7
Alveologenic carcinoma	0	1	0	0
Hemangioma	0	6	1	2
Squamous cell carcinoma	0	2	0	0
Lymphosarcoma	2	0	0	3
Reticulum cell sarcoma	0	0	0	0
Total number of tumors	6	25	5	12

[a] The number of animals submitted for histopathologic examination included all animals sacrificed at the conclusion of the investigation and any post-mortem animal or animals sacrificed *in extremis* with signs of possible tumor formation. All other animals were examined grossly and found to be free of tumors or tumor-like growth.

Source: Reyna (1973).

Mutagenic Effects

Mutagenesis studies have been carried out using Charles River strain albino mice as test animals. A dominant lethal mutation study was conducted with technical grade carbofuran by Arnold (1971). An untreated control, a positive control, methyl methanesulfonate and 2 levels of treatment with carbofuran (0.25 and 0.5 mg/kg) were utilized in the test. Twelve males were included in each treatment group including the controls. Each male was mated to 3 females per week for 6 weeks. The females were sacrificed 1 week after removal from the breeding cage and were examined for implantation sites, resorption sites, and embryos.

Data for the first 2 weeks of the positive control group indicated that a dominant lethal mutation had occurred. The data from the control and carbofuran treatment groups revealed that no dominant lethal mutation was present in these animals (Arnold, 1971).

Teratogenic Effects

Teratogenesis studies were conducted using New Zealand albino rabbits. A total of 40 female rabbits were observed for 60 days before testing. Four groups of 10 females each were placed on test according to the following protocol:

Group	Test material	Dose level (mg/kg of body weight) per day	Number of females per group
Control	None[a]	-	10
Positive control	Thalidomide	75.0	10
Test Group I	Carbofuran	0.1[b]	10
Test Group II	Carbofuran	0.5	10

a/ Control group females received a sham dose (empty gelatin capsule).
b/ Technical grade carbofuran
Source: Jackson (1968).

Treatments were given on day 6 through day 18 of the gestation period. On gestation day 29, all females were sacrificed and the litters recovered by caesarian section. After 24 hr of observation for viability, the fetuses were sacrificed and examined by dissection. Particular attention was given to the skeletal tissue and the differences in size, shape, and position of major organs and blood vessels. A positive thalidomide control group was included to indicate teratogenic sensitivity of the rabbit strain used.

Examination of 120 fetuses from females treated with carbofuran revealed no gross abnormalities. Internal structural formation was normal and skeletal development was well defined. The young were present in normal numbers, were well formed, and showed good survival during the first 24 hr after Caesarian delivery. However, the incidence of resorption was twice as high in both carbofuran test groups as in the control group (Jackson, 1968).

Other Toxicity Tests

Eye Irritation - Rabbits - Palazzolo (1963c) conducted a study on eye irritation using New Zealand white rabbits. Technical carbofuran (5 mg) was instilled into the conjunctival sac of the right eyes of 2 rabbits; the left eyes were used as controls. Examinations were then made at intervals up to 7 days.

After 10 min, both rabbits exhibited miosis which persisted for 2 hr. Thereafter, the condition cleared. Only minimal irritation was reported in this test (Palazzolo, 1963).

Skin Sensitivity - Guinea Pigs - Technical carbofuran injected intracutaneously into the skin of male guinea pigs did not elicit a sensitizing reaction. Injections were given every other day for 20 days. The first injection was 0.05 ml and all others were 0.10 ml each. The challenge dose was given 2 weeks following the 10th injection (Schoenig, 1967g).

Neurotoxicity - Chickens - When treated with a concentration of technical carbofuran equal to the LD_{50} concentration of 38.9 mg/kg, white Leghorn hens dosed with technical carbofuran exhibited salivation and general weakness, but not leg and wing weakness at a concentration equivalent to the LD_{50} (38.9 mg/kg). In surviving birds, the weakness subsided in 24 hr. Surviving birds were given another acute dose at 21 days with similar results. No physical signs of delayed neurotoxicity (demyelination) were observed and, therefore, microscopic examinations were not performed (Jackson, 1967).

Potentiation Studies - Sprague-Dawley rats were the test animals used in potentiation studies. Schoenig (1966) determined the LD_{50} of carbofuran and other pesticides (12 compounds), and then determined the LD_{50} of equitoxic mixtures of carbofuran and each of the other compounds. The results were compared to theoretical LD_{50} values derived from assumption of strictly additive toxicity. Potentiation of the acute oral toxicity of carbofuran by any of the other test materials was not observed. For example, the theoretical LD_{50} of an equitoxic mixture of carbofuran and ethion was 104.1 while the observed LD_{50} was 180. The theoretical LD_{50} of a mixture of carbofuran and Sevin was 129.1 and the observed LD_{50} was 111.0. The ratio of theoretical to observed LD_{50} was 0.58 for ethion and carbofuran, and 1.16 for Sevin and carbofuran (Schoenig, 1966).

Symptomology and Pathology

Signs of Toxicity - Signs of intoxication that developed in rats after an acute dose of carbofuran were reported by various investigators as follows: fibrillary action, salivation, ataxia, lacrimation, exophthalmos, hyperpnea, cyanosis, hemorrhagic conjunctivitis, tonic-clonic convulsions, diuresis, labored breathing, sprawling of the limbs, and depression. The dosage resulted in the deaths of some animals (Palazzolo, 1963; [illegible], and Palazzolo, 1963c).

The signs observed in the dog were similar to those seen in the rat. The predominant reactions reported for a single acute dose of carbofuran were tremors (lasting 4 to 6 hr) emesis and moderate to severe convulsions. The dose resulted in the deaths of some animals (Baran, 1967a).

Signs of subacute intoxication are coughing, gagging, salivation, muscular tremors, and emesis (Baran, 1966).

The most frequently observed signs of acute intoxication with carbofuran in sheep and cattle were reported by Palmer and Schlinke (1973) to be increased salivation, lolling tongue movements, stiff uncoordinated gait, dyspnea, muscular tremors, ataxia, and prostration. Acute intoxication might also prove to be fatal.

Signs reported for acute intoxication in chickens include salivation, general weakness, and a specific extreme leg and wing weakness (Jackson, 1967).

Symptoms of Toxicity - In humans the symptoms of carbofuran intoxication are assumed to be those produced by other cholinesterase inhibitors: headache, nervousness, blurred vision, general weakness, nausea and cramps, diarrhea, sweating, tearing, excessive respiratory tract secretion, cyanosis, convulsions, coma, loss of reflexes, loss of sphincter control, and cardiac arrest. Carbofuran intoxication can also cause death (Hayes, 1963).

Treatment of Intoxication

Sprague-Dawley rats with a body weight of 150 g were administered technical carbofuran orally at concentrations of 3.5 and 5.3 mg/kg. Within 30 seconds after dosing with the insecticide, atropine sulfate (1.5% solution) was given intraperitoneally.

Animals which were not given atropine exhibited salivation, lacrimation, miosis, and generalized tremors. Those treated with atropine exhibited only generalized tremors. At a dose of 3.5 mg/kg carbofuran, 25% of the rats died; animals treated at 3.5 mg/kg carbofuran plus 50 mg/kg atropine had a mortality of 8.3%. Rats dosed at 5.3 mg/kg of carbofuran followed by treatment with atropine sulfate at 100 mg/kg had a mortality of 6.2%, while the test animals at 5.3 mg/kg carbofuran exhibited mortality equal to 69% (Palazzolo, 1963a).

Sprague-Dawley albino rats weighing 175 g were administered technical carbofuran at 5.3 mg/kg. Thirty seconds after treatment, 2-pyridine aldozime methochloride (2-PAM Cl) was given to 2 groups of carbofuran-treated animals at 100 or 150 mg/kg. Eighty percent of the carbofuran controls and 60% of both groups given 2-PAM Cl treatment died. These results appeared to indicate that 2-PAM Cl cannot be recommended as treatment for carbofuran intoxication. In addition, the animals which received only 2-PAM Cl exhibited reactions of dyspnea, exophthalmos, excitation, and mild generalized tremors 5 to 30 min following dosing. These symptoms persisted for about 1-1/2 hr (Palazzolo, 1964a).

Treatment of dogs with atropine sulfate was also found to reduce reactions due to treatment with technical carbofuran (5.3 mg/kg). Two dogs were treated with atropine sulfate (50 mg) when symptoms of intoxication appeared. Severe reactions occurred for 3 hr in the absence of an atropine treatment. Dogs treated with 50 mg atropine sulfate responded immediately (Palazzolo, 1963d).

New Zealand strain albino rabbits were given a single dose of technical carbofuran by gavage and, as soon as signs of intoxication appeared, half of the test animals were given an injection containing 10 mg of atropine sulfate. The atropine-treated animals responded immediately. Symptoms of intoxication persisted in the nontreated animals for 5 hr. Seventy-five percent of the non-atropine-treated rabbits died, but none of the atropine-treated animals succumbed (Palazzolo, 1964b).

Calves, 1 to 2 weeks old, were treated orally with technical carbofuran at doses from 0.25 mg to 5 mg/kg.

When signs of toxicosis appeared, animals which had received doses of 1 and 5 mg/kg carbofuran were treated with atropine sulfate peritoneally at a dosage of 0.5 mg/kg body weight. The animal administered 1 mg/kg carbofuran died even though treated with atropine sulfate; the animal dosed with carbofuran at 5 mg/kg and treated with atropine sulfate survived. The authors did not comment on the results (Palmer and Schlinke, 1973).

Sheep were administered carbofuran at 5 and 10 mg/kg body weight. When signs of toxicosis were observed, 3 animals treated at 5 mg/kg and 1 animal treated at 10 mg/kg were treated intravenously with atropine sulfate at a dose of 0.5 mg/kg body weight. The animals that received 5 mg/kg carbofuran survived; the animal given 10 mg/kg carbofuran died even though treated with atropine sulfate (Palmer and Schlinke, 1973).

For treatment of organophosphorus pesticide poisoning in man, Hayes (1963) recommends a dosage of 1 to 2 mg atropine sulfate at the appearance of symptoms. In cases where excessive secretions occur, the individual should be given atropine sulfate every hour up to 50 mg a day.

The recommendation made in the *Merck Manual* (1966) for organic phosphate poisoning is 1 to 4 mg of atropine intramuscularly or intravenously, followed by 1 to 2 mg every 20 min up to a total of 10 to 20 mg/day.

Accidental Exposures

Accidental exposures to carbofuran are recorded by the EPA Pesticide Episode Review System (PERS). Computerized PERS data for the period 1972 through January 1974 showed carbofuran to be the twenty-sixth most frequently cited compound in the review system. More recently, a review was conducted of the PERS data for the period January 1967 to April 1975 (EPA, 1975). This review indicated that a total of 55 episodes had been reported, including those involving humans, animals, plants, and contaminated areas. However, in most cases, carbofuran was not conclusively established as the cause of the episode. There was substantial evidence to link the pesticide to the episodic effect for only 3 of the 26 episodes involving accidental human exposure. The available data was too limited to establish any relationship between the episodes and any specific method of application or use of carbofuran.

The geographical distribution of the 55 episodes, according to EPA Region, is as follows:

EPA region	No. of episodes
1	0
2	1
3	1
4	6
5	4
6	6
7	7
8	13
9	14
10	3

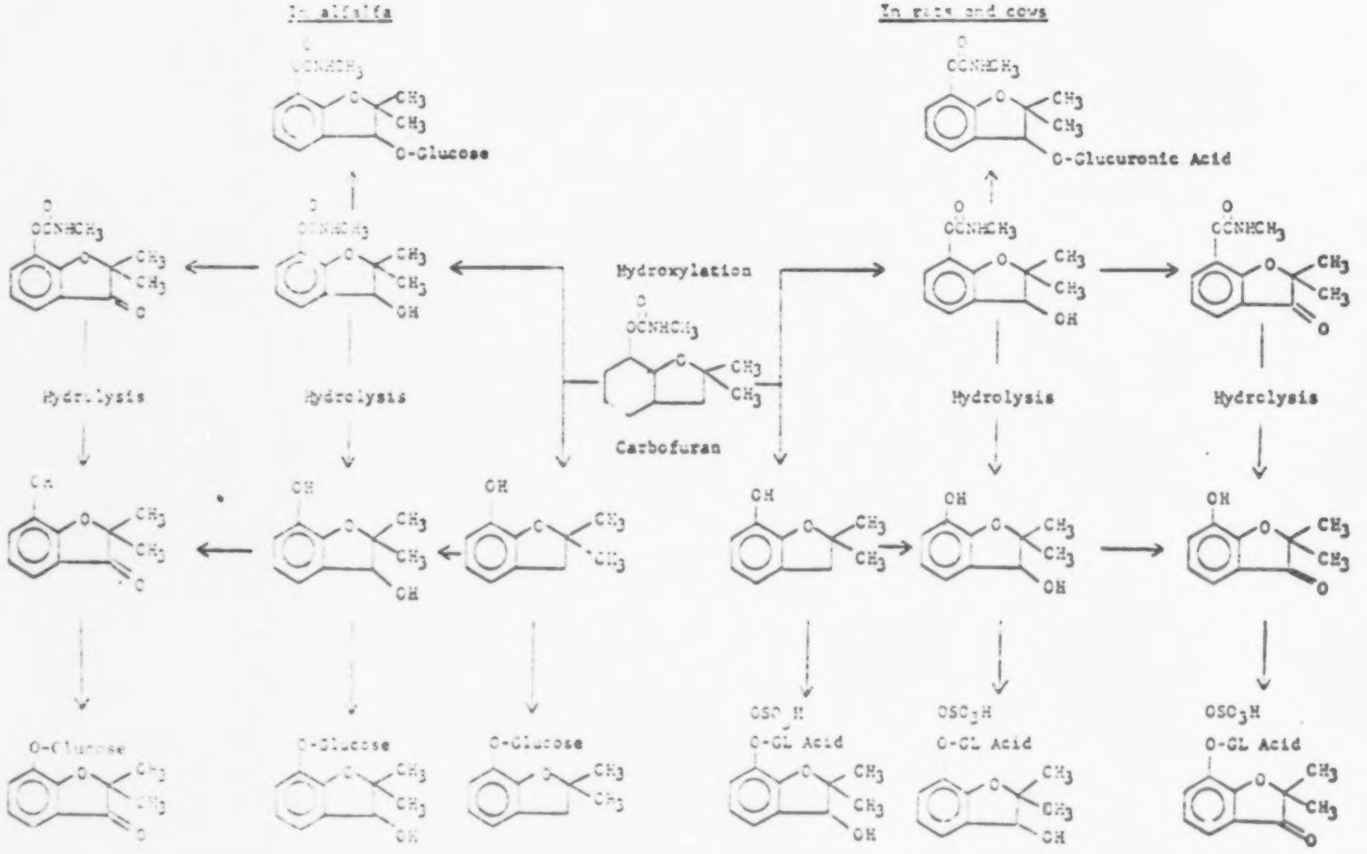
Metabolism

The main pathway of oxidative metabolism of carbofuran in plants, insects, and animals appears to consist of hydroxylation at the benzylic carbon to yield 3-hydroxycarbofuran (see Table 19 and Figure 7). The hydroxylated product is further oxidized to give 3-ketocarbofuran. Hydrolysis and conjugation then occur. The 3-keto compound is hydrolyzed at a much faster rate than the parent carbofuran although hydrolysis and conjugation can also occur at other stages of metabolism. Carbofuran can be converted (hydrolyzed) to 2,3-dihydro-2,2-dimethyl-7-hydroxybenzofuran (carbofuran phenol) or hydroylsis can follow oxidation to 3-hydroxycarbofuran.

The available data appears to indicate that hydrolysis is preceded by oxidative metabolism (Schlagbauer and Schlagbauer, 1972; Metcalf, 1968; Casida and Lykken, 1969; O'Brien, 1967; and Ryan, 1971).

Numerous studies describing the specific steps in the metabolic pathways of carbofuran in plants and animals are cited in Table 17. The products of oxidation and hydrolysis of carbofuran in rats, cows, and in plants, as proposed by Knaak (1971), are shown in Figure 7.

Insect Metabolism - Microsomal preparations of housefly tissues were used by Metcalf et al. (1968) to study the effects of mixed function oxidases on carbofuran. The results of this study suggested that carbofuran is hydroxylated at 4 sites: the 3-position of the furan ring, the 6-position of the aryl ring, the N-methyl group and the 2-methyl groups. The authors stated, however, that formation of substantial amounts of metabolites hydroxylated at the N-methyl or 2-methyl groups does not appear likely.



Source: Knaak, G. B. 1971. Biological and nonbiological modifications of carbamates. Bull. World Health Org. 44:121-131. Reprinted by permission of the World Health Organization.

Figure 7. Proposed Products of Carbofuran Oxidation and Hydrolysis

Table 17. Metabolites of Carbofuran

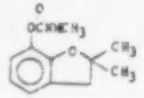
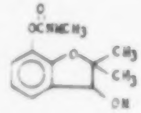
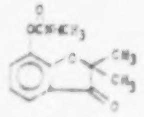
Name of compound usually found in the literature	Formula	Probable metabolic reaction resulting in formation	Plants and animals in which metabolite has been found	References
Carbofuran (I)		Pesticidal compound could also be secondarily released from (XII)	Mammals, birds, fish Insects, plants, soil	Schlegbauer and Schlagbauer (1972) Casida and Lykken (1969); O'Brien (1967) Ryan (1971); Knaak (1971); Fukuto (1972); Menzie (1969); Wustner et al. (1974); Menn (1972); Kuhr (1970)
3-Hydroxycarbofuran (II)		Aromatic hydroxylation of (I) (Oxidative)	Rat	Lucier (1972); Dorough (1968b)
			Chicken	Hicks et al. (1970)
			Cattle	Ivie and Dorough (1968); Knaak et al. (1970b); Miles et al. (1971)
			Mouse	Metcalf (1968)
			Cotton	Metcalf et al. (1968)
			Alfalfa	Knaak et al. (1970a)
			Corn	Turner and Caro (1973); Caro et al. (1973); Metcalf et al. (1968)
			Beans	Dorough (1968a)
			Tobacco	Ashworth and Sheets (1972)
			Pine	Free and Saunders (1974)
			Insects	Black et al. (1973); Shrivastava et al. (1971); Metcalf (1968); Sangha (1971)
			Earthworms	Stenersen et al. (1973)
			Soil	Caro et al. (1973)
3-Ketocarbofuran (III)		Oxidation of (II)	Rat	Dorough (1968b); Lucier et al. (1972)
			Cattle	Ivie and Dorough (1968)
			Mouse	Metcalf et al. (1968)
			Cotton	Metcalf et al. (1968)
			Alfalfa	Knaak et al. (1970b)
			Corn	Caro et al. (1973); Turner and Caro (1973); Metcalf et al. (1968)
			Beans	Dorough (1968a)
			Tobacco	Ashworth and Sheets (1972)
			Insects	Shrivastava et al. (1971); Sangha (1971); Metcalf (1968)
			Soil	Caro et al. (1973)

Table 17. (Continued)

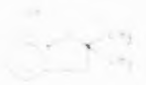
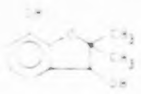
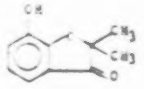
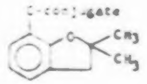
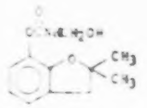
Name of compound and designation	Formula	Probable metabolic reaction resulting in formation	Plant or animal in which metabolite has been found	References
Carbofuran phenol (IV)		Hydrolysis of (I)	Corn Rat Cattle Mouse Cotton Alfalfa Beans Tobacco Insects Pine	Metcalf et al. (1968) Dorough (1968b); Lucier et al. (1972) Knaak et al. (1970b); Ivie and Dorough (1968) Metcalf et al. (1968) Metcalf et al. (1968) Knaak et al. (1970a) Dorough (1968a) Ashworth and Sheets (1972) Metcalf et al. (1968) Free and Saunders (1974)
3-Hydroxycarbofuran phenol (V)		Hydrolysis of (II)	Rats Chicken Cattle Alfalfa Beans and tobacco Insects Earthworms Cotton Pine	Lucier et al. (1972) Hicks et al. (1970) Ivie and Dorough (1968); Knaak et al. (1970b) Knaak et al. (1970a) Ashworth and Sheets (1972); Dorough (1968a) Metcalf et al. (1968) Stenersen et al. (1973) Metcalf et al. (1968) Free and Saunders (1974)
3-Ketocarbofuran phenol (VI)		Hydrolysis of (III) or oxidation of (V)	Rat Chicken Cattle Mouse Alfalfa Corn Beans Tobacco Pine Insects Cotton	Dorough (1968b); Lucier et al. (1972) Hicks et al. (1970) Ivie and Dorough (1968); Knaak et al. (1970b) Metcalf et al. (1968) Knaak et al. (1970a) Metcalf et al. (1968) Dorough (1968a) Ashworth and Sheets (1972) Free and Saunders (1974) Metcalf et al. (1968) Metcalf et al. (1968)
Carbofuran phenol conjugate (VII)		Conjugation of (IV)	Rat Cattle Mouse Cotton Alfalfa Tobacco Insects	Dorough (1968b) Knaak et al. (1970b) Metcalf et al. (1968) Metcalf et al. (1968) Knaak et al. (1970a) Ashworth and Sheets (1972); Metcalf et al. (1968) Metcalf et al. (1968)

Table 17. (Continued)

Name [illegible]	Formula	Primary metabolic reaction resulting in formation	Plants and animals in which metabolite has been found	References
[illegible]		Conjugation of [illegible]	Cattle Mouse Alfalfa Corn Tobacco	Knaak et al. (1970b) Metcalf et al. (1968); Black et al. (1973) Knaak et al. (1970a) Metcalf et al. (1968) Ashworth and Sheets (1972)
[illegible]		Conjugation of [illegible]	Cattle Mouse Alfalfa Corn	Knaak et al. (1970b) Metcalf et al. (1968); Black et al. (1973) Knaak et al. (1970a) Metcalf et al. (1968)
[illegible]		Aliphatic hydroxylation of [illegible] or aromatic hydroxylation of [illegible] (oxidative)	Rat Chicken Mouse Beans Insects Cattle Cotton	Dorough (1968b); Lucier et al. (1972) Hicks et al. (1970) Black et al. (1973) Dorough (1968a) Dorough (1968a) (1968b) Ivie and Drough (1968) Metcalf et al. (1968)
N-Methylolcarbofuran (XI)		Aliphatic hydroxylation of (I) (oxidative)	Chicken Mouse Pine Insects	Hicks et al. (1970) Metcalf et al. (1968) Pree and Saunders (1974) Dorough (1968b); Metcalf et al. (1968)
[illegible]		Conjugation of [illegible] can be metabolized to [illegible]	Rat	Dorough (1968b)

Plant Metabolism - The following studies summarize available information on the metabolism of carbofuran in specific crops. The ratios of major carbofuran metabolites in 6 crops are given in Table 18.

Isolated cotton leaves were allowed to imbibe labeled carbofuran and then, at intervals up to 12 days, representative samples were homogenized, extracted, and chromatographed. Total recovery of radioactivity ranged from 80 to 94% in the leaf homogenates (Metcalf et al., 1968).

Two-dimensional thin layer chromatography (TLC) of leaf extracts resulted in detection of the following metabolites: carbofuran phenol, 3-hydroxycarbofuran, 3-hydroxycarbofuran phenol, 3-ketocarbofuran, 3-ketocarbofuran phenol, and conjugates of the phenolic and alcoholic metabolites. In this study conjugates of N-methylolcarbofuran were not detected.

Exposure of the conjugates to β-glucosidase enzymes (emulsion) resulted in liberation of the aglycones (3-hydroxycarbofuran phenol, 3-ketocarbofuran phenol) showing that these plant conjugates were glucosides (Metcalf et al., 1968). Only a small quantity of the 3-hydroxycarbofuran conjugate could be released by either enzymates or acid digestion.

The metabolites formed by the intact cotton plant were demonstrated to be similar to those formed in isolated leaves. However, the rate of metabolism in the intact plant was more rapid than in isolated leaves (Metcalf et al., 1968).

The metabolism of carbofuran was studied in isolated corn leaves and in corn seedlings. The isolated leaves were allowed to imbibe the insecticide, but the seedlings were grown from seeds treated topically.

Table 18. Ratios of Carbofuran Metabolite Residues in 6 Major Crops

Plant	Major metabolite	Phenol/carbamate ratio
Potato	Carbofuran phenol	8/1
Corn (foliage)	Phenols	3/1
Alfalfa	3-Hydroxycarbofuran	1/1
Sugar beet (foliage)	3-Ketocarbofuran phenol	1/1
Tomato (vine)	3-Hydroxycarbofuran	1/2
Bean plant (bean)	3-Hydroxycarbofuran	1/16

Source: FMC Corporation (1971).

The rate of metabolism in isolated corn leaves was slower than the rate in isolated cotton leaves, but the conjugate metabolites appeared to be the same for the 2 plants.

TLC revealed the presence of 3-hydroxycarbofuran and 3-ketocarbofuran phenol in the leaves together with the phenolic conjugates. The roots were found to contain large proportions of carbofuran phenol and lesser amounts of 3-hydroxycarbofuran and 3-ketocarbofuran (Metcalf et al., 1968).

The metabolism of carbofuran in corn plants was also studied by Turner and Caro (1973). The investigators reported that over 90% of the carbofuran was converted to 3-hydroxycarbofuran and 3-ketocarbofuran by the time the plants reached silage stage. Most of the residue in leaves (92 to 93%) was 3-hydroxycarbofuran. The author also reported that, in the corn stalks, the principal metabolic process was hydrolysis to 3-hydroxycarbofuran with no accompanying oxidation.

Metabolites of carbofuran were isolated from roots and tops of tobacco plants by Ashworth and Sheets (1972) in studies on root and foliar uptake of the insecticide.

Neither carbofuran nor its unconjugated metabolites were found to accumulate in the roots of the tobacco plants. In addition, only trace amounts of glycosidic aglycones (3-hydroxycarbofuran) were detected after acid hydrolysis of the methanol-soluble root extracts.

Analyses from root-uptake studies of the tops of tobacco plants, however, showed that the expected metabolites were present — carbofuran phenol, 3-ketocarbofuran phenol, 3-ketocarbofuran, 3-hydroxycarbofuran, and several unidentified compounds.

Some differences were noted by these investigators when the results of analyses from root-uptake studies were compared to foliar-uptake studies. Carbofuran was not found in plant parts other than the treated leaves. The hydrolysis product, carbofuran phenol, was the major unconjugated metabolite.

In the root-uptake studies, the oxidation product 3-hydroxycarbofuran was most abundant. From studies with topically applied material the investigators also concluded that most of the carbofuran does not penetrate plant cuticle and is therefore not subjected to metabolic processes in the plant.

The half-life of carbofuran absorbed through the root system and in the leaves of tobacco plants was approximately 4 days. Carbofuran and the oxidation products, 3-hydroxycarbofuran and 3-ketocarbofuran, were hydrolyzed to their corresponding phenols. The hydroxy compounds were eventually conjugated as glycosides.

Bean plants (Dorough, 1968a) and animals (Dorough, 1968b) were reported to produce the same metabolic products of carbofuran. The metabolite present in highest concentration was 3-hydroxycarbofuran. This material was found as the free carbamate, but its concentration never equaled its concentration as a water-soluble conjugate. The compounds 3-ketocarbofuran and 3-hydroxy-N-methylolcarbofuran, both free and conjugated, were also detected in the plants. In a test using ^{14}C ring-labeled carbofuran, the hydrolytic products carbofuran phenol, 3-hydroxycarbofuran phenol, and 3-ketocarbofuran phenol were isolated.

Of the hydrolytic products, only carbofuran phenol was found in the free form, but always at a concentration below the soluble conjugated form.

The metabolism in the potato of radio-labeled carbofuran (^{14}C ring-labeled and ^{14}C carboxyl-labeled) was also investigated. Carbofuran was applied to the soil around 60-day-old field plants and to the soil around greenhouse plants. The greenhouse potatoes were harvested 7 days later and the field potatoes 60 days later.

Using greenhouse plants, the following glycosides were found after 7 days: carbofuran phenol (45% of metabolites); 3-ketocarbofuran phenol (6.8%); 3-hydroxycarbofuran phenol (4.2%); and 3-hydroxycarbofuran (26.2%). Carbofuran and 3-hydroxycarbofuran were also found at respective levels of 9.2 and 6.4%.

Using field-grown plants, the following glycosides were found after 60 days: carbofuran phenol (71.5% of metabolites); 3-ketocarbofuran phenol (8.6%); 3-hydroxycarbofuran phenol (3.8%); and 3-hydroxycarbofuran (11.5%).

Extraction, hydrolysis and chromatographic studies indicated that carbofuran was absorbed by the potato roots and was transferred to the tubers prior to hydrolysis and conjugation. The ^{14}C carboxyl label remained in the tubers and became a part of the natural product (Knaak, 1970b).

The residue content and metabolism of carbofuran was also investigated in field-grown tomato plants. One-week-old plants were treated with the equivalent of 2.2 lb/acre of radio-labeled ^{14}C-carbofuran and sampled for analysis at 11 days (immature) and 50 days (mature) after treatment.

Total ^{14}C residues in mature and immature (tomato) vines were 1.15 and 1.58 ppm (ring-^{14}C) and 0.33 and 1.0 ppm (carbonyl-^{14}C) at the respective intervals. Total ^{14}C-residues in mature and immature fruit were 0.08 and 0.07 ppm (ring-^{14}C) and 0.04 and 0.18 ppm (carbonyl-^{14}C). Mature and immature roots exhibited a total ^{14}C-content of 15.98 and 9.44 ppm (ring-^{14}C) and 26.42 and 7.60 ppm (carbonyl-^{14}C).

Carbofuran was metabolized in the plant by oxidation to form 3-hydroxycarbofuran (33.0% in mature vine and 35.7% in immature vine). More carbofuran was found in the immature (28.3%) than in the mature (2.6%) vine. The major phenolic component was 3-ketocarbofuran phenol (19.9% mature and 12.1% immature).

In mature root the major metabolite was 3-hydroxycarbofuran (52.2%); in immature root, the carbofuran was the major component (46.4%).

In tomato fruit, the ^{14}C levels of activity were too low to permit an accurate evaluation of possible metabolites (Munger, 1972).

Twelve 35-day-old sugar beet plants were placed within barriers and, at 65 days, 4 plants were administered 18.0 mg/plant ^{14}C ring-labeled carbofuran and 4 were administered 18.0 mg/plant carbonyl ^{14}C-carbofuran. Four untreated plants were selected as controls. One-half of the treated and the control plants were harvested at 30 days and the remainder at 72 days.

Carbofuran was readily absorbed into the sugar beet roots and was translocated to foliage. The major carbamate metabolite identified was 3-hydroxycarbofuran while the predominant phenol was 3-ketocarbofuran phenol (Robinson, 1972).

Carbofuran was applied to the soil of potted alfalfa plants (9 mg/pot of ^{14}C ring-labeled carbofuran), and after a 30-day growth period, the plants were harvested and analyzed for carbofuran metabolites.

The major metabolites identified (Knaak et al., 1970b) were the glycosides of 3-hydroxycarbofuran (37.3%), 3-hydroxycarbofuran phenol (18.5%), and 3-ketocarbofuran phenol (20%). Total residue uptake expressed as carbofuran amounted to 76 ppm.

The roots of Mugho pine shrubs (30 to 45 cm in height) were exposed for 24 days to a solution of ^{14}C carbonyl or ^{14}C ring-labeled carbofuran. The needles were collected at various dates and were analyzed for metabolites along with the buds, roots, trunk, and current wood growth of the shrubs. (Pree and Saunders, 1974).

An unidentified metabolite and 3-hydroxycarbofuran were the only organo-soluble metabolites detected in the plant fraction from trees treated with carbonyl-^{14}C carbofuran. Accumulation of metabolites was greatest in the needles.

In the trees treated with ^{14}C ring-labeled carbofuran, carbofuran phenol was the main organo-soluble in each sample, although 3-hydroxycarbofuran and 3-ketocarbofuran phenol were also found. Two unidentified metabolites [illegible] also present.

The separation of carbofuran and its true metabolites from their conjugated forms indicated that most of the metabolites were in the conjugated form, although all compounds were also present in the free form. Treatment with β-glucosidase or β-glucuronidase [illegible] of the identified metabolites from the conjugated form to the free form.

Metabolism in Mammals

Male Swiss white mice were given ra.io-labeled carbofuran (^{3}H-labeled, 1.68 mc/mmole), and over the following 24-hr period, urine was collected and analyzed for metabolites. Two mice treated orally with 2 mg/kg of the ^{3}H-labeled carbofuran eliminated 37 and 67% of the administered radioactivity in the 24-hr period.

The major metabolite, 3-hydroxycarbofuran, was detected in the urine by an ether extraction procedure. Smaller amounts of 3-ketocarbofuran and carbofuran phenol were also identified. The major conjugate and aqueous portion was of 3-ketocarbofuran phenol.

The metabolism of carbofuran in mice was shown to be similar to that in plants and insects; however, more of the carbofuran dose was metabolized by mice to the water-soluble 3-hydroxycarbofuran than was true for plants or insects (Metcalf et al., 1968). In plants, 3-hydroxycarbofuran; in mice nearly 45% of the radio-label recovered in metabolites was present in 3-hydroxycarbofuran.

Carbofuran metabolites formed by the soluble fraction of rat liver homogenates were identified by Dorough (1968b) as 3-hydroxy-N-methylolcarbofuran, N-methylolcarbofuran, 3-hydroxycarbofuran, 3-hydroxycarbofuran phenol, 3-ketocarbofuran phenol and carbofuran phenol. Three unidentified compounds and other water-soluble complexes were also found. The metabolites formed and their relative concentrations are shown in Table 14.

The 3-hydroxy-N-methylolcarbofuran, when incubated singly with liver 15,000 g solubles, was largely converted to water-soluble materials (conjugates). Both N-methylolcarbofuran and 3-hydroxycarbofuran were reported to have been metabolized (a) to an unidentified fraction (2.2 and 0.6%, respectively), (b) to 3-hydroxy-N-methylolcarbofuran (6.9 and 8.9%), (c) to 3-hydroxycarbofuran phenol (4.1 and 3.9%, respectively), and (d) to water soluble materials (23.9 and 23.4%, respectively)

Carbofuran phenol was metabolized by the rat liver enzymes system primarily to conjugated, water-soluble compounds.

The in vivo metabolism in rats was studied by housing treated animals in metabolic cages and collecting and analyzing urine and feces separately. Analysis of the organo-extractable metabolites in urine indicated that in vivo metabolism was similar to in vitro metabolism with liver homogenates. Two metabolites, 3-ketocarbofuran phenol and an unknown, were not detected in the unconjugated form in the rat urine, but they were present as water-soluble conjugates. Four additional metabolites were also produced from the water-soluble conjugates by means of acid hydrolysis: 3-hydroxy-N-methylolcarbofuran, 3-hydroxycarbofuran, 3-hydroxycarbofuran phenol, and carbofuran phenol.

Radioactivity in the water fraction from 14C-ring-labeled carbofuran incubation was about 3 times greater when microsomes from control rats were used than when microsomes from methylmercury hydroxide-treated rats were used.

Rats treated with methylmercury hydroxide excreted carbofuran-^{14}-C equivalents more rapidly than controls.

The metabolites obtained from the treated animals were identified as 3-hydroxycarbofuran, carbofuran phenol, 3-hydroxycarbofuran phenol, 3-ketocarbofuran, 3-hydroxy-N-methylolcarbofuran, and N-methylolcarbofuran.

Table 19. Degradation of Labeled Carbofuran by Rat Liver 15,000 G Solubles

	% of radioactivity added	
	Carbonyl-labeled ^{14}C	Ring-labeled ^{14}C
Unknown I	0.07	0.10
Unknown II	0.011	0.09
Unknown III	0.05	0.03
3-OH-N-Methylolcarbofuran	1.76	2.07
N-Methylolcarbofuran	6.40	7.05
3-OH-Carbofuran	21.09	20.13
3-OH-Carbofuran phenol	0.00	0.02
3-ketocarbofuran phenol	0.00	0.02
Carbofuran phenol	0.00	3.82
Water solubles	5.89	7.01
Carbofuran	60.29	58.50

Source: Adapted from Dorough (1968b).

Prior treatment of rats with either methylmercury hydroxide or chlordane affected the rate at which microsomal fractions from the rat's liver would metabolize carbofuran. However, the treatment did not alter the type of metabolite which resulted (Lucier et al., 1972).

The excretion of carbofuran metabolites in cows' milk was studied by Dorough and Ivie (1968). Two percent of an oral dose (gelatin capsule of ^{14}C-carbonyl-labeled carbofuran, 2.7 mg) was eliminated in milk, but only 0.16% of a ^{14}C-ring labeled dose was detected. The investigators noted a distinctly different distribution of the radioactivity from that found with other carbamates. Significant quantities of labeled residues could not be extracted from milk, and most of the residues extractable by organic solvents could not be extracted from lipid materials. This suggested that some of the radioactivity in milk from cows fed ^{14}C-carbonyl labeled carbofuran was not in metabolites, but in naturally occurring chemicals that had incorporated the ^{14}C atom from the treatment.

Another study by Ivie and Dorough (1968) included only ^{14}C-labeled carbofuran, but also ^{14}C-labeled sodium bicarbonate. Results from these tests supported the earlier idea that the greater ^{14}C-carbonyl-labeled residue resulted from incorporation of $^{14}CO_2$ into body chemicals normally found in milk. The authors calculated that only 0.31% of the radioactive dose of ^{14}C-carbonyl-labeled carbofuran was eliminated in the milk as extractable metabolites. With the extractable metabolites from milk, traces of parent carbofuran were present along with 3-hydroxycarbofuran, 3-ketocarbofuran, 3-hydroxy-N-methylolcarbofuran, 3-hydroxycarbofuran phenol, 3-ketocarbofuran phenol, and one unidentified metabolite. The 3 metabolites (3-hydroxycarbofuran, 3-ketocarbofuran phenol, and carbofuran phenol) were the products in highest concentration (70 to 80%).

The metabolism of carbofuran residues in alfalfa fed to cows was studied by Knaak et al. (1970b). The carbofuran residues present in the alfalfa were identified as carbofuran and the glycosides of 3-hydroxycarbofuran, carbofuran phenol, 3-hydroxycarbofuran phenol, and 3-ketocarbofuran phenol. Since these materials were all present in the alfalfa at the time of feeding, metabolic pathways could not be defined. These residues were metabolized and excreted as sulfates of 3-ketocarbofuran phenol, carbofuran phenol, and 3-hydroxycarbofuran phenol.

The overall process was reported to include hydrolysis of the glycosides and the carbomates, oxidation of the phenols, and conjugation of the resulting compounds with sulfuric or glucuronic acid.

Cows were also treated with ^{14}C-carbonyl-labeled carbofuran by Miles et al. (1971) and the milk from these animals was analyzed for metabolites.

When cows were administered carbofuran, either by gelatin capsule or by feeding in silage, the only metabolite reported in the milk was 3-hydroxycarbofuran. Its concentration ranged from nondetectable to 0.26 ppm in the milk from 8 cows, averaging 0.13 ppm (Miles et al., 1971). An average of 0.05% of the administered dose was excreted in the milk as 3-hydroxycarbofuran. Ivie and Dorough (1968) reported that carbofuran and at least 6 metabolites were detected in milk from carbofuran-treated cows.

Metabolites excreted in the fecal material of laying hens given ^{14}C-carbonyl-labeled carbofuran and ^{14}C-ring-labeled carbofuran were detected by Hicks et al. (1970). The authors found that rapid hydrolytic degradation occured. After 6 hr 54% of the dose had been hydrolyzed; by 24 hr, 72% had been hydrolyzed. Five unidentified metabolites were detected along with 3-hydroxycarbofuran, N-methylolcarbofuran, 3-hydroxy-N-methylolcarbofuran, 3-ketocarbofuran, and carbofuran phenol. The predominant metabolite was 3-hydroxycarbofuran phenol.

The concentration of carbofuran metabolites in eggs was low. Maximum radioactive residue in eggs from hens treated with ^{14}C-ring-labeled carbofuran was 0.13 ppm.

Samples of liver, kidney, gizzard, heart, breast, thigh, leg, skin, brain, fat, and blood were collected and were analyzed for radioactive residues. All tissues at both 6 and 24 hr contained ^{14}C-carbofuran equivalents; none were detected after this time in hens treated with ^{14}C-ring-labeled carbofuran. However, some residues were detected in tissues from hens treated with ^{14}C-carbonyl-labeled carbofuran after 3 days. There was no proof, however, that the radioactivity detected was actually present as label in carbofuran or carbofuran metabolites.

Free and conjugated forms of 3-hydroxy-N-methylolcarbofuran and N-methylolcarbofuran were found in the liver. Analyses of gizzard tissue revealed the presence of carbofuran, 3-hydroxycarbofuran, 3-hydroxy-N-methylolcarbofuran and an unidentified metabolite.

Metabolism in soil - In a study on persistence of carbofuran in soil, Caro et al. (1973) found that after application of carbofuran to the soil, partial conversion of the pesticides to the oxidation product, 3-ketocarbofuran, occurred. However, only traces of the product, 3-hydroxycarbofuran, were found in soil samples. In corn grown on the treated soil, over 90% of the parent carbofuran was detected as 3-hydroxycarbofuran in the stalks.

Cholinesterase inhibition

A comparative study using carbofuran, 3-hydroxycarbofuran and 3-ketocarbofuran as inhibitors of cholinesterase indicated that in rats all compounds were generally ineffective inhibitors at a concentration of 1 x 10^{-3} µg/ml (Lazanas, 1967). However, in dogs, both carbofuran and 3-hydroxycarbofuran caused greater than 50% inhibition at 1 x 10^{-3} µg/mg, while 3-ketocarbofuran only resulted in 26.9% inhibition.

The concentration of inhibitor (µg/ml) resulting in 50% inhibition of erythrocyte cholinesterase in dogs was 1 x 10^{-5} for carbofuran and between 1 x 10^{-4} and 1 x 10^{-4} and 1 x 10^{-5} for 3-hydroxycarbofuran. The results of these tests are summarized as follows:

Inhibitor	concentration of inhibitor (µg/ml)	% Inhibition of erythrocyte cholinesterase	
		Dog	Rat
Carbofuran	1 x 10^{-3}	65.5	22.2
3-Hydroxycarbofuran	1 x 10^{-3}	67.2	21.7
3-Ketocarbofuran	1 x 10^{-3}	26.9	21.7

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART C. FATE AND SIGNIFICANCE

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This section contains data on the environmental effects of carbofuran, including its effects on aquatic species, wildlife, and beneficial insects. The interactions of carbofuran with lower terrestrial organisms and its residues in soil and water are also discussed. The section summarizes rather than interprets the data reviewed.

Effects on Aquatic Species

Fish -

Laboratory Studies - The toxicity of technical carbofuran to fish reported in different tests (see Table 20) appeared to vary depending upon the species of fish tested and on the conditions prevailing at the time of testing.

Longnose killifish (*Fundulus similis*) were not affected by doses of technical carbofuran up to 0.1 ppm, but sheepshead minnow (*Cyprinodon variegatus*) were irritated by 0.1 ppm carbofuran. However, the killifish were irritated when exposed to Furadan 3G at 10 lb/acre for 48 hr; 10% mortality occurred within 24 hr when exposed to Furadan 3G at 20 lb/acre. The fish recovered when placed in clean water (Lowe, 1970).

A study by Schoenig (1967) indicated that rainbow trout, channel catfish, and bluegill were of about equal sensitivity to technical carbofuran and that the 96 hr TL_m ranged from 0.21 to 0.28 ppm for these 3 species (Table 20).

The 24 hr LC_{50} of technical carbofuran to channel catfish was reported to be 2.03 ppm by Carter and Graves (1973) under static conditions of testing, a value 10 times higher than that reported by Schoenig (1967) for channel catfish also tested under static conditions.

In a test conducted by Carter (1971) on channel catfish, it was also reported that the amount of carbofuran required to effect a 50% reduction in cholinesterase activity was 0.19 ppm. Treated fish showed the following sequential signs of toxicity: hypoactivity, lethargy, body paralysis, scoliosis, loss of equilibrium, opercular and mouth paralysis followed by death.

The signs and symptoms of toxicity that appeared in 3 species of fish during tests to determine the TL_m of a formulation (Furadan® 10G) were reported by Schoenig (1967) as follows:

Rainbow trout: 96 hr TL_m = 4.0 ppm

Signs at:	1 ppm	No signs observed.
	1.8 ppm	Hypoactivity.
	3.2 ppm	Hypoactivity, increased respiration, and intermittent loss of equilibrium.
	5.6 ppm	Hypoactivity, intermittent loss of equilibrium, convulsions, gasping mouth, distended operculum, increased respiration.

Channel catfish: 96 hr TL_m = 4.1 ppm

Signs at:	1 ppm	No signs noted.

	1.8 ppm	Hypoactivity, increased respiration, intermittent loss of equilibrium.
	3.2, 5.6, and 10.0[a/] ppm	Hypoactivity, increased respiration, intermittent loss of equilibrium, flaccidity (intermittent), convulsions, gasping mouth, distended operculum.

Bluegill: 96 hr TL_m = 2.3 ppm

Signs at:	1.0 ppm	No signs noted.
	1.8 ppm	Hypoactivity, increased respiration, intermittent loss of equilibrium, intermittent flaccidity, intermittent convulsions
	3.2 and 5.6 ppm	Same as 1.8.

[a/] At this level, all fish were dead within 3 hr.

Field Studies - The U.S. Department of the Interior's Denver Wildlife Research Center (Flickinger, 1975) studied the effects of carbofuran on fish and other nontarget organisms in several areas in Texas where it was used to control larvae of the rice water weevil, Lissorhoptrus oryzophilus.

When carbofuran (as 3% granules) was applied to rice fields at the rate of 0.5 lb AI/acre, some mortality of mosquito fish (Gambusia affinis) occurred 1 hr after treatment. Heavy mortality of mosquito fish, large-scale menhaden (Brevoortia patronus), Atlantic croaker (Micropogon undulatus), and European carp (Cyprinus carpio) was found 24 and 48 hr after treatment.

In the rice fields where these observations were made, rice seeds were treated with another insecticide. It is not known if and to what extent the insecticide in seed treatment may have contributed to the fish mortalities observed.

Table 20. Toxicity of Technical Carbofuran and Its Formulations to Fish

Fish species	Formulation tested	Exposure time (hr)	Toxicity calculation	Toxicity measured	References
Channel catfish (Ictalurus punctatus)	Tech.	24	LC_{50}	2.03 ppm (-)	Carter (1971)
Channel catfish (Ictalurus punctatus)	Tech.	24	LC_{50}	2,030 µg/ℓ (-)	Carter and Graves (1973)
Yellow perch (Perca flavescens) City water	Tech.	24	LC_{50}	150 µg/ℓ (126-179)	Mauck (1972)
Yellow perch (Perca flavescens) City water	Tech.	96	LC_{50}	147 µg/ℓ (115-187)	Mauck (1972)
Bluegill (Lepomis macrochirus)	Tech.	96	LC_{50}	80 µg/ℓ (-)	Carter and Graves (1973)
Mosquito fish (Gambusia affinis)	Tech.	96	LC_{50}	300 µg/ℓ (-)	Carter and Graves (1973)
Fathead minnow (Pimephales promelas) City water	Tech.	24	LC_{50}	1,320 µg/ℓ (991-1,760)	Mauck (1972)
Fathead minnow (Pimephales promelas) City water	Tech.	96	LC_{50}	1,180 µg/ℓ (814-1,710)	Mauck (1972)

Table 20. Toxicity of Technical Carbofuran and Its Formulations to Fish (Continued)

Fish species	Formulation tested	Exposure time (hr)	Toxicity calculation	Toxicity measured	References
Steelhead trout (*Salmo gairdneri*) Standard water	Tech.	24	LC_{50}	1,020 μg/ℓ (635-1,640)	Mauck (1972)
Steelhead trout (*Salmo gairdneri*) Standard water	Tech.	96	LC_{50}	600 μg/ℓ (436-826)	Mauck (1972)
Brown trout (*Salmo trutta*)					
City water	Tech.	24	LC_{50}	355 μg/ℓ (262-521)	Mauck (1972)
Standard water	Tech.	24	LC_{50}	862 μg/ℓ (705-1,010)	Mauck (1972)
Brown trout (*Salmo trutta*)					
City water	Tech.	96	LC_{50}	280 μg/ℓ (205-383)	Mauck (1972)
Standard water	Tech.	96	LC_{50}	560 μg/ℓ (475-660)	Mauck (1972)
Lake trout (*Salvelinus namaycush*)	Tech.	24	LC_{50}	164 μg/ℓ (119-226)	Mauck (1972)
Lake trout (*Salvelinus namaycush*)	Tech.	96	LC_{50}	164 μg/ℓ (119-226)	Mauck (1972)
Coho salmon (*Oncorhynchus kisutch*) Standard water	Tech.	24	LC_{50}	530 μg/ℓ (432-650)	Mauck (1972)
Coho salmon (*Oncorhynchus kisutch*) Standard water	Tech.	96	LC_{50}	526 μg/ℓ (-)	Mauck (1972)
Rainbow trout (*Salmo gairdneri*)	10 G	96	TL_m	4.0 ppm (2.5-6.1)	Schoenig (1967)
Channel catfish (*Ictalurus punctatus*)	10 G	96	TL_m	4.1 ppm (2.4-7.0)	Schoenig (1967)
Bluegill (*Lepomis macrochirus*)	10 G	96	TL_m	2.3 ppm (1.7-2.9)	Schoenig (1967)
Rainbow trout (*Salmo gairdneri*)	Tech.	96	TL_m	0.28 ppm (0.23-0.35)	Schoenig (1967)
Channel catfish (*Ictalurus punctatus*)	Tech.	96	TL_m	0.21 ppm (0.16-0.28)	Schoenig (1967)
Bluegill (*Lepomis macrochirus*)	Tech.	96	TL_m	0.24 ppm (0.18-0.34)	Schoenig (1967)

Extensive search of the literature and contacts with several laboratories known to be engaged in fish toxicity studies with pesticides failed to produce additional reports on the effects, if any, of carbofuran on fish under field conditions.

Commercial labels of carbofuran 10% granules carry the following warning regarding fish toxicity:

> This product is toxic to birds, fish, shrimp, crab and other wildlife. Birds and other wildlife in treated areas may be killed. Keep out of lakes, streams, ponds, tidal marshes and estuaries. Cover or incorporate granules which are spilled during loading and which are exposed on the soil surface in turn areas. Do not apply where runoff is likely to occur. Do not contaminate water by cleaning of equipment or disposal of wastes.

A similar warning is included in the labeling of the carbofuran 4 lb AI/gal flowable formulations.

Typical labels of carbofuran 2, 3 and 5% granules state: "This product is toxic to fish and wildlife; keep out of lakes, streams, or ponds. Keep irrigation water out of lakes, streams, and ponds for at least 7 days."

Lower Aquatic Organisms -

Laboratory Studies - Carter and Graves (1973) studied the acute toxicity of several commonly-used insecticides (including carbofuran) to several species of fish, to the white river-crawfish, and to bullfrog tadpoles. The crawfish were seined from roadside ditches near the Louisiana State University and placed into large aluminum pans with a capacity of 2.5 l. The bullfrog tadpoles were obtained by seining ponds of the Louisiana State University Fisheries Unit on the Ben Hur Plantation and tested in aquaria lined with polyethylene bags. Statis bioassay tests were carried out in tap water (pH 7.0, hardness of 2 to 5 ppm) that was aged and aerated for at least 2 days. The bioassay procedures, conditions, and results were as follows:

Procedure, condition and results	White river-crawfish	Bullfrog tadpole
Mean weight of test animals, g	0.7	3.4
Number of animals per container	3	10
Replications per dose	5	2
Exposure time, hr	96	96
Test container volume, liters	0.5	20
Water temperature, C	26	23-26
Dissolved oxygen, ppm	9-11	6-9
LC_{50}, ppb	500	2,700

The LC_{50}'s of the other insecticides included in these studies ranged from 2 to 50,000 ppb for the crawfish, and from 270 to 185,000 ppb for the bullfrog tadpole. The crawfish was more sensitive to all insecticides tested than the bullfrog tadpole. In comparison to the other insecticides, carbofuran ranged intermediate in toxicity to both test animals.

In model ecosystem studies (reported in greater detail in the section on Bioaccumulation and Biomagnification), Sangha (1972) and Yu et al. (1974) found that carbofuran was highly toxic to the lower aquatic organisms with which the test tanks were stocked, including fresh water clams (Corbicula manilensis), fresh water crabs (Uca minax), frogs (species not identified), snails (Physa species), and water fleas (Daphnia magna). Most of these organisms were killed shortly after sorghum plants growing on the terrestrial part of the system were treated with carbofuran at a rate equivalent to 1 lb AI/acre. Fresh aquatic organisms were reintroduced into the test tanks every 5 to 7 days. Those stocked 20 days after the application of carbofuran survived. The authors did not report the concentration of carbofuran in the water during this period. Sangha (1972) stated that the LC_{50} of carbofuran to Daphnia was found to be 20 ppb.

Technical carbofuran did not appear to affect the eastern oyster (Crassostrea virginica) in 24-, 48-, and 96-hr tests of up to 1.0 ppm carbofuran. However, technical carbofuran and Furadan 3G were highly toxic to pink shrimp (Penaeus duorarum). The 24-, and 48-hr EC_{50} values for the shrimp exposed to technical carbofuran were 0.0068 and 0.0046 ppm, respectively. Furadan 3G at 15 lb/acre caused 70% paralysis or mortality of the shrimp within 24 hr (Lowe 1970).

Field Studies - In the previously mentioned field studies on the effects of the use of carbofuran 3% granules on rice (Flickinger, 1975), there was heavy mortality of cricket frogs, crayfish, earthworms, and nontarget aquatic insects which occurred generally between 1 and 45 hr after treatment. No details regarding the degree of mortality or the nontarget species involved are given in the unpublished progress reports available at this time.

Effects on Wildlife

Laboratory Studies - The oral LD_{50} of carbofuran ranged from 0.238 mg/kg to 5.04 mg/kg in 8 species of adult birds. The fulvous tree duck was most sensitive and the bobwhite quail was most resistent (see summary of toxicity in Table 21). Dermal toxicity was studied with 2 species (Quelea quelea and Passer domesticus) and in both cases was reported to be 100 mg/kg (Schafer et al., 1973).

The age of mallard ducks was shown to affect their response to carbofuran although the difference in the LD_{50} between the most sensitive age group and the most resistant age group was only about twofold (Hudson et al., 1972). The greatest susceptibility to carbofuran appeared to occur at hatching or shortly thereafter and decreased to the minimum value around 1 week of age. The susceptibility then appeared to increase to 30 days of age and began again to approach maximum susceptibility at 6 months of age.

Table 21. Acute Toxicity of Carbofuran to Birds

Species	Formulation tested	Toxicity calculation	Toxicity measured	References
Ring-neck pheasant (3 months) (Phasianus colchicus)	Tech.	LD_{50} (oral)	4.15 mg/kg (2.38-7.22)	Tucker and Crabtree (1970)
Mallard duck (3-4 months) (Anas platyrhynchos)	Tech.	LD_{50} (oral)	0.397 mg/kg (0.315-0.500)	Tucker and Crabtree (1970)
Mallard duck (Anas platyrhynchos)				
36-hr old	Tech.	LD_{50} (oral)	0.370 mg/kg (0.283-0.484)	Hudson et al. (1972)
7-days old	Tech.	LD_{50} (oral)	0.628 mg/kg (0.530-0.744)	Hudson et al. (1972)
30-days old	Tech.	LD_{50} (oral)	0.510 mg/kg (0.410-0.635)	Hudson et al. (1972)
6-months old	Tech.	LD_{50} (oral)	0.415 mg/kg (0.333-0.516)	Hudson et al. (1972)
Fulvous tree duck (3-6 months) (Dendrocygna bicolor)	Tech.	LD_{50} (oral)	0.238 mg/kg	Tucker and Crabtree (1970)
Bobwhite quail (Colinus virginianus)	Tech.	LD_{50} (oral)	5.04 mg/kg (3.64-6.99)	Tucker and Crabtree (1970)
Japanese quail (M) (2 weeks) (Coturnix japonica)	Tech.	LD_{50} (oral)	1.9 mg/kg (1.7-2.1)	Sherman and Ross (1969)
Japanese quail (F) (2 weeks) (Coturnix japonica)	Tech.	LD_{50} (oral)	1.7 mg/kg (1.3-1.9)	Sherman and Ross (1969)
Quelea (Quelea quelea)	Tech.	LD_{50} (oral)	0.42 mg/kg (-)	Schafer et al. (1973)
House sparrow (Passer domesticus)	Tech.	LD_{50} (oral)	1.3 mg/kg (-)	Schafer et al. (1973)
Red-wing blackbird (Agelaius phoeniceus)	Tech.	LD_{50} (oral)	0.42 mg/kg (-)	Schafer et al. (1973)
Quelea (Quelea quelea)	Tech.	LD_{50} (dermal)	100 mg/kg (-)	Schafer et al. (1973)
House sparrow (Passer domesticus)	Tech.	LD_{50} (dermal)	100 mg/kg (-)	Schafer et al. (1973)

The sequential signs of poisoning for Japanese quail administered technical carbofuran were lethargy, ataxia, quivering, and death. When death did not occur, lethargy usually lasted 24 hr (Sherman and Ross, 1969).

Similar signs and symptoms of acute poisoning were reported for mallards, pheasants, and bobwhite quail by Tucker and Crabtree (1970). The authors observed the following signs to be associated with acute toxicity: ataxia, wings crossed high over back, nutation, diarrhea, phonation, salivation, lacrimation, immobility with wings spread, dyspnea, miosis, terminal wingbeat convulsions or opisthotonos. Symptoms in survivors persisted up to 7 days. Mortalities occurred as soon as 5 min after treatment.

Subacute toxicity of carbofuran to Japanese quail was studied by Sherman and Ross (1969). Rations containing 50, 100, 200, 400 and 800 ppm carbofuran were fed ad libitum to groups of quail (20/group) for 6 weeks. The feed consumption, weight gain, and mortality were recorded over the entire feeding period. The results indicated that carbofuran was not toxic at dietary levels of 200 ppm or less, but was highly toxic when fed at 400 ppm or more for the 6-week feeding period. Feed efficiency was affected significantly at levels greater than 200 ppm.

Although there appeared to be no sex difference in susceptibility to a single oral dose, the male appeared more susceptible to continued subacute doses. At the highest level fed (800 ppm) some females survived to the third week while all males died during the first week. At 400 ppm all males died by the fourth week while one-third of the females survived the entire 6-week feeding period. During the feeding experiment, eggs were collected from females over a 17-day period after reaching the egg-producing age. The results indicate that fertility and hatchability were greatly depressed at levels of 200 ppm and higher. No abnormal embryos were observed among the fertile eggs failing to hatch, and there were no abnormalities observed among the newly hatched quail.

Hudson (1972) studied subacute toxicity of technical carbofuran administered orally by gelatin capsules to ring-necked pheasants. A group of 3 cocks and 3 hens, 20 or 25 weeks old, were exposed daily for 30 days to 2.10 and 4.20 mg/kg/day. No mortality occurred at the lower rate. At 4.20 mg/kg/day, 1 male died after 8 doses, and 1 female died after 3 doses. Weight loss of 41 g was observed at 2.10 mg/kg/day and 75 g at 4.20 mg/kg/day during the first week of treatment. The birds began to gain weight by the second week. By the end of the 30-day period, weight gains in the pheasants were similar to the controls.

Signs which appeared most severe during the first several days of treatment included ataxia, hyperexcitability, tremors, jerkiness, tenseness, ataraxia, high carriage, hypoactivity, running and falling and chronic convulsions. Brain acetylcholinesterase in the dead birds was inhibited 47.6%; survivors of both levels showed little or no inhibition.

Symptoms of carbofuran toxicity to bobwhite quail, ring-necked pheasants, Japanese quail and mallard ducks exposed to technical carbofuran and Furadan

10G (Gough and Shellenberger, 1972) were mild lethargy, hypoactivity, regurgitation, and lacrimation; at higher levels terminal wing-beat convulsions and partial paralysis were observed prior to death. Following necropsy, mild to moderate hemorrhagic areas in the lung, stomach, esophagus, and crop were observed in those birds found dead as a result of treatment. Surviving birds generally appeared normal 3 to 4 days following treatment. The results of other studies on subacute toxicity are summarized in Table 22. The mallard duck appeared to be more susceptible to the toxic action of carbofuran than either pheasant or Japanese quail.

Field Studies - The U.S. Department of Interior's Denver Wildlife Research Center (Flickinger, 1975) studied the effects of applications of carbofuran to rice fields on a number of wildlife species, including birds. Observations were made in 3 Texas study areas in 1970 and 1973 after applications of carbofuran 3% granules to rice fields at the rate of 0.5 AI/acre. Species of birds found dead or sick at 17 and 24 hr after treatment were western sandpiper (Ereunetes mauri), pectoral sandpiper (Erolia melanotos), and red-winged blackbird (Agelaius phoeniceus). The western sandpiper was found to be the species most susceptible to carbofuran. All dead sandpipers contained from 1 to 8 carbofuran granules in their stomachs. Mortality of all birds thus was believed to be largely the result of consumption of the carbofuran-treated granules, although it was pointed out that in the study area, rice seeds were treated with another insecticide.

A field test was conducted by Harris and Applewhite (1969) to assess the hazard of carbofuran to mallard ducks when applied as Furadan 3G under conditions representing pre-flood rice application. Twelve pairs of adult mallards (a pair consisting of one drake and one hen) were used for each formulation. Furadan 2G was applied at the rate of 25 lb/acre, 16 hr before water was allowed to enter the field, and Furadan 3G at 20 lb/acre. Daily feedings consisted of 8 oz of cracked corn scattered in the water. After 14 days of observation no mortality or adverse affects were seen in any of the mallard ducks.

Furadan 10G was tested under field conditions simulating normal application procedure to a prepared seed bed. Its effect upon adult bobwhite quail at rates of 20, 60 and 200 lb/acre was studied. After the 5-week experimental period, no marked adverse effects on body weight of males and females were observed other than fluctuations in weekly average body weights. Two males died at the 60 lb/acre level and 2 males at the 200 lb/acre level. Intestinal enteritis was thought to be the cause of these 4 deaths. One-half of the surviving males and females were necropsied and evidence of an intetstinal enteritis was observed in several birds of all treatment levels. It was not established that Furadan 10G was the cause of the intestinal enteritis (Shellenberger, 1971).

In a field study with 14 pairs of 12-week-old ring-necked pheasants exposed to Furadan 75 WP at a rate of 1.3 lb/acre (1.0 AI/acre) for 14 days, Stephens (1969) observed no mortality or adverse effects in any of the test groups.

In another field study, Zorb (1971) found similar results with Furadan 75 WP. Sprays of 1.0 lb/acre were applied directly on pheasants, food or

Table 22. Subacute Toxicity of Carbofuran to Birds

Species	Formulation tested	Days exposure	Toxicity calculation	Toxicity measured (ppm) expressed in (95% confidence limits)	References
Ring-neck pheasant	10G	7	LC_{50}	9,600 (775-13,598)	Jackson (1968)
(*Phasianus colchicus*)	Tech.	5	LC_{50}	438 (356-529)	Hill (1974)
	Tech.	5	LC_{50}	573 (492-666)	Stickel (1975)
Mallard duck	10G	7	LC_{50}	2,100 (1,455-3,034)	Jackson (1968)
(Anas platyrhynchos)	Tech.	5	LC_{50}	190 (156-230)	Hill (1974)
	Tech.	5	LC_{50}	190 (156-230)	Stickel (1975)
Bobwhite quail	10G	7	LC_{50}	10,250	Jackson (1968)
Japanese quail	Tech.	5	LC_{50}	438 (356-529)	Hill (1974)
(*Coturnix japonica*)	Tech.	5	LC_{50}	437 (356-529)	Stickel (1975)
	Tech.	6 (weeks)	LC_{50}	200-400	Sherman & Ross (1969)

vegetation, and combinations of these 3 treatments. Pheasants that died had high infestations of internal parasites. It was not established whether the Furadan or the parasite killed the birds. There were no apparent effects on reproduction in the treated birds that had received an application 8 months before and during egg laying. The author concluded that Furadan 75 WP causes no ill effects on pheasants.

Carbofuran at 0.2 lb AI/acre was applied to a 5 acre pond in the Kern National Wildlife Refuge in California to simulate control of mosquito larvae. Birds on or around the pond included sandpiper, killdeer, blackbirds, meadowlarks, horned larks and lark sparrows. On an adjacent pond of the refuge there were pintail, teal, sandpipers, dowitchers and yellow legs. There was no evidence of dead or affected wildlife (Hagen,1971).

Field Investigations - The U.S. Environmental Protection Agency's Pesticide Episode Review System (PERS) contains 3 reports of carbofuran episodes involving birds during the period January 1967 to April 1975 (EPA, 1975).

In 1972, a "bird kill" (not further defined) in Wisconsin was ascribed to carbofuran. However, the report on this episode states that no evidence exists to link carbofuran to the bird kill. A survey of 60 fields revealed only 1 owl with (unspecified) pesticide residues.

In 1972 in California, 19 geese were found ill, and 15 of them died in an alfalfa field 24 hr after application of carbofuran (formulation and rate not given). The episode report states, however, that insufficient evidence exists to link carbofuran to this incident.

On March 15, 1974, in California, 2,450 widgeon ducks, 2 Canadian geese, and 1 mallard duck died in an alfalfa field located near a reservoir. The alfalfa had been treated with carbofuran (4 lb AI/gal flowable formulation) to control the Egyptian alfalfa weevil (*Hypera brunneipennis*). Laboratory analysis revealed that the deaths were not caused by a disease, and carbofuran was present in the crops of the sample birds. Local officials felt that the presence of large numbers of birds was due to an unusual delay in migration. It was concluded that, in this case, substantial evidence existed linking carbofuran to the bird kill.

The label of Furadan® 4 flowable, a liquid formulation containing 4 lb of carbofuran AI/gal, carries the following warning regarding bird toxicity: "This product is toxic to fish, birds and other wildlife. Birds feeding on treated areas may be killed."

The label for carbofuran 10% granular bears the following statement regarding bird toxicity:

> This product is toxic to birds, fish, shrimp, crab and other wildlife. Birds and other wildlife in treated areas may be killed. Keep out of lakes, streams, ponds, tidal marshes and estuaries. Cover or incorporate granules which are spilled during loading and which are exposed on the soil surface in turned areas.

Labels for carbofuran 2, 3, and 5% granular formulations state: "This product is toxic to fish and wildlife . . . . Birds feeding on treated areas may be killed."

Effects on Beneficial Insects

Bees - Bailey and Swift (1968) and Anderson et al. (1971), based on laboratory and field data, classified carbofuran as "highly toxic" to honeybees. The term "highly toxic" was defined as including severe losses which "may be expected if the pesticide is used when bees are present at treatment time or within a day thereafter."

These bee toxicity ratings are based on laboratory studies by Atkins et al. (1973), as well as on more than 120 large-scale field tests on crops in bloom and highly attractive to honeybees (Anderson et al.,1971). Most tests were run on alfalfa, and a few were made on ladino clover, cotton, sweet corn, and in peach and citrus orchards. The test insecticides were applied by airplane or by power ground sprayers. The publication by Anderson et al. (1971) does not include experimental details pertaining specifically to the testing of carbofuran in this program.

Atkins et al. (1973) summarized the results of toxicity tests in which a large number of pesticides and other agricultural chemicals were studied with regard to their effects on the honeybee (Apis mellifera). In a laboratory procedure which primarily measures a chemical's contact effect, pesticides were applied in dust form to groups of 25 bees per test dose, 3 replicates per each of 3 colonies, for a total of 9 replicates per test dose. This procedure permits determination of an LD_{50} value for each pesticide in micrograms of chemical per bee. Honeybees (worker bees of uniform age obtained from the same colony before treatment) were exposed to carbofuran for 48 hr at 80°F (26.7°C) and 65% relative humidity. Under these conditions, the LD_{50} of carbofuran was 0.15 µg/bee, placing it into Group I, "highly toxic to honeybees."

In their test procedures, Atkins et al. (1973) also determined the slope of the dosage-mortality curve for each pesticide tested, and recorded it as a "slope value" in terms of probit units. Pesticides with a slope value of 4 probits or higher can often be made safer to honeybees by lowering the dosage only slightly. Conversely, by increasing the dosage only slightly, the pesticide can become highly hazardous to bees. Carbofuran rated a slope value of 4.31, indicative of a moderately steep dosage-mortality curve.

Atkins et al. (1970) studied the effects of a carbofuran application at the rate of 1.0 lb AI/acre on seed alfalfa on the Santiaga Ranch in Kern County, California, in 1968. Carbofuran was applied as a spray in 10 gal of water per acre by airplane to a non-replicated 16-acre plot in a field in good bloom which contained 2 to 3 well-established colonies of bees per acre. The treatment was made directly over the unprotected test bee colonies. Effects of the treatment were determined from records of honeybee kill at the hive and in field cages, colony strength and behavior, and field bee blossom visitation rates. Observations were made for several days before, the day of, and for 4 to 5 days after treatment. Dead bee records at the colonies were obtained by daily counts of bees collected in traps placed on 6 colonies per treatment. Cages of bees were placed in the fields at fly-over time to measure the initial contact effect. Other cages of bees were placed in the treated areas at intervals after treatment to study residual fumigation. Average summer weather conditions prevailed during the test period.

Field bee visitation returned to normal after a drastic reduction for 5 days following carbofuran application. There was no significant kill in trapped colonies placed in the carbofuran-treated field, 4, 7, or 10 days after treatment. The carbofuran treatment killed 100% of the caged bees exposed during treatment, but there were no fumigation effects at 1 to 2 hr post-treatment. The authors concluded that bee colonies can be safely placed in carbofuran-treated fields 4 days after treatment.

Field Reports on Bee Toxicity - The U.S. Environmental Protection Agency's Pesticide Episode Review System contains several reports of injury to bees attributed to carbofuran during the period January 1967 to April 1975 (EPA,1975).

On June 12, 1972, all honeybees in 36 hives were destroyed in Utah after the application of carbofuran to a nearby alfalfa field, No further information was given regarding application details, or how the bees were exposed. The episode report states that insufficient evidence existed to link carbofuran to this bee kill.

On March 27, 1973, a bee kill (not further defined) occurred in California, apparently caused by bees carrying contaminated pollen back to the hives where a progressive kill occurred. No details are given regarding the crop or type of carbofuran application involved, and carbofuran was not verified as the causative agent.

On June 1, 1973, in Wyoming, 192 honeybee colonies were "moderately damaged" (no further details given) after carbofuran had been applied to a nearby field to control alfalfa weevils. Formulation, method, and rate of application were not given. Seven apiaries were involved. The episode report states that insufficient evidence existed to link carbofuran to the bee damage.

Three additional episodes involving damage to bee colonies in Wyoming in June of 1973 have been reported. In 1 case, 89 honeybee colonies from 2 apiaries were moderately damaged. In another case, 63 honeybee colonies were damaged severely, and 11 colonies were damaged moderately; 3 apiaries were involved. In the third case, 33 bee colonies from 1 apiary were moderately damaged. In all 3 instances, carbofuran was applied to nearby fields for the control of alfalfa weevils. No details regarding the carbofuran applications or the manner of exposure of the bees were given. Carbofuran was not verified as the causative agent in any of these episodes.

On August 12, 1974, in Montana, 25 beehives were "affected" when bees had to pass through a corn field recently treated with carbofuran (treatment details not given) in order to reach an alfalfa field. There were 300 to 400 dead bees found lying around each hive. The episode report stated that circumstantial evidence existed linking carbofuran to the incident.

The commercial label for Furadan® 4 flowable (containing 4 lb of carbofuran AI/gal) includes the warning: "Do not move bees into alfalfa fields within 7 days of application."

No bee toxicity statements are found in the labeling of carbofuran granular formulations.

Beneficial Parasites and Predators - Croft and Meyer (1973) studied the toxicity of carbofuran to 3 different strains of the phytoseiid mite, *Amblyseius fallacis*, a common predator of spider mites in commercial fruit orchards in central and eastern United States and Canada. Carbofuran 75% wettable powder was tested against an organophosphate-resistant strain from Hartford, Michigan, a strain selected with carbaryl for 9 yr, and a strain selected with carbofuran for 4 yr. The LC_{50}'s of carbofuran as determined by a laboratory leaf-dip technique were 0.002 lb for the first strain and 0.006 lb for the latter 2. This data indicates that there was no appreciable development of resistance of the predator to carbofuran.

Elsey (1973) investigated the effects of carbofuran and several other insecticides on the spined stilt bug, *Jalysus spinosus*, a foliage-inhabiting predator of insect eggs and aphids on tobacco. Carbofuran 10% granules were applied at the rate of 6 lb AI/acre as a broadcast treatment before tobacco was transplanted. Treated and untreated plots were randomized and replicated 3 times. The density of stilt bug adults in the carbofuran-treated plots was slightly lower than in the check plots throughout the season, though the differences were seldom statistically significant at the 5% level by Duncan's multiple range test. The populations of stilt bug nymphs were much lower, and nymphs were seldom found in the plots treated with carbofuran. Since some stilt bug adults and eggs remained in the carbofuran-treated plots throughout the season, the investigators attributed the lack of nymphs to the poisoning and death of eggs or newly-hatched nymphs which fed on treated plant tissue or came in contact with carbofuran residues brought to the leaf surface by trichome exudates. Other predators were present but not abundant in the plots, and there were no statistical differences between treated and untreated plots.

On 4 different dates in August, each of the test plots was infested with 30 eggs of the tobacco budworm, *Heliothis virescens*, from a laboratory culture by gluing 3 eggs per plant to the underside of leaves on 10 plants in the center 2 rows of each plot. The plants were checked after 48 hr for indications of insect predation, and for missing and normal eggs. Egg losses caused by predators with chewing mouthparts were not included. In this test, the predation of budworm eggs in the carbofuran-treated plots was significantly lower than in the check plots (at the 5% level by Duncan's multiple range test) on 3 of the 4 test dates.

Interactions with Lower Terrestrial Organisms

Flora - The effects of carbofuran and 3 other nematicides on microorganisms in soil were studied by Tu (1972) in experiments conducted with Delhi loamy sand, a typical agricultural soil in southwestern Ontario. The soil contained 0.81% organic matter and 0.03% nitrogen, and had a moisture-holding capacity of 27%, and pH of 8.2. Carbofuran was added to the soil at the rates of 1 and 5 µg/g of soil. Reagent grade peptone and elemental sulfur powder were added to the soil samples at 1,000 µg of nitrogen or sulfur per g to measure ammonification and sulfur oxidation, respectively. Oxidation of ammonium from soil organic nigrogen was studied by nitrification. The experimental mixtures and controls were held in 0.5 pint milk bottles closed with polyethylene film. Soil moisture was maintained at 60% of capacity. The treatments, in duplicate, were incubated 1 week in the laboratory at 28°C for ammonification, 1 and 2 weeks for nitrification, and 4 weeks for sulfur oxidation. Changes in population of soil microorganisms were determined after 1, 2, 4, 8, and 12 weeks.

Plate count data indicated that neither carbofuran nor any of the other 3 nematicides affected fungal population drastically. Five µg/g of carbofuran slightly depressed fungal population 1, 2, and 4 weeks into the experiment. At 8 and 12 weeks, there were no significant differences in the fungal counts between carbofuran treatments and untreated controls. The higher rate of carbofuran significantly decreased bacterial populations during the first week of incubation, but they subsequently recovered to levels at or above those found in the controls. Plate counts in the controls showed a decrease in fungal and bacterial populations during the 12-week incubation period. The carbofuran treatments generally had no significant effects on ammonification or nitrification of ammonium from soil organic nitrogen. Oxidation of elemental sulfur was depressed significantly by both carbofuran treatments.

Tu (1972) also measured the soil microbial respiration using the Warburg technique. Oxygen consumption from decomposition of native organic matter was greater in the carbofuran treated soils than in the controls. Oxygen consumption increased as carbofuran concentrations were increased in soils with and without supplemented glucose-carbon. The author concluded that indigenous soil microorganisms can tolerate carbofuran and the other nematicides tested.

In further experiments with the same soil and with carbofuran at the same rates (1 and 5 ppm), Tu (1973) added temperature as another variable. Treated soil samples were incubated at 5 and 28°C. Fungal and bacterial populations were counted 2, 14, 28, and 56 days after incubation, soil respiration with and without glucose was measured, and effects of the treatments on ammonification and nitrification were determined. Carbofuran again did not significantly affect bacterial or fungal counts, ammonification, nitrification, mineralization of soil organic sulfur, or oxidation of mineral sulfur. The carbofuran treatments did not significantly decrease oxygen consumption from the decomposition of indigenous soil organic matter at either temperature. However, there was a marked respiration increase in soils without supplemental glucose-C at 30°C with the 5 ppm carbofuran concentration. The author ascribed this to readjustments of microflora and ascendancy of certain groups and species following the depression of competitors and antagonists, resulting in increased microbial activity.

Harnish and Wendler (1972) investigated the effects of carbofuran on oxygen uptake by microorganisms in the soil. Topsoil treated with Furadan 10G at a rate of 100 ppm and 10 ppm AI was added to flasks (100 g of soil per flask). Sufficient water was introduced to bring the samples to 60% of their moisture-holding capacity. Using a Gilson Differential Respirometer and standard manometric techniques, oxygen uptake was observed for an incubation period of 85 hr.

The data in Table 23 indicates that Furadan 10G at 100 and 10 ppm AI had no noticeable influence on soil respiration. Oxygen uptake in both Furadan treatments was slightly higher than the untreated check. The authors suggest this could indicate "slight degradation of carbofuran or one of the components in the formulation."

Table 23. Effect of FURADAN 10G on Oxygen Uptake in Field Soil

	Oxygen Uptake (µl) at Specified Incubation Period[b]				
Substrate[a]	1 Hr	2.5 Hr	4.5 Hr	60 Hr	85 Hr
FURADAN 100 ppm	66	36.4	45.2	43.4	44.2
FURADAN 10 ppm	3.0	32.8	34.0	30.8	32.4
GLUCOSE 200 ppm	30.2	108.4	152.6	172.2	229.8
FURADAN 100 ppm + GLUCOSE 200 ppm	37.8	104.0	139.6	161.6	198.4
FURADAN 10 ppm + GLUCOSE 200 ppm	31.2	92.2	127.0	138.6	186.6
Untreated	0.0	22.2	24.0	11.2	20.5

[a] FURADAN applied as 10% Granules, rate expressed in ppm active ingredient carbofuran.

[b] Incubated at 25°C; 5 g soil.

Source: Harnish, W. N., S. J. Wendler, FMC Corporation, in Studies of the impact of carbofuran on the environment, 1972.

When glucose was added to the untreated soil, respiration was stimulated, indicating metabolism of the substrate by soil microorganisms. The addition of Furadan 10G to the soil containing glucose had little effect on soil respiration.

Lin et al. (1972) studied the effects of carbofuran and several other insecticides on soil nitrification, growth of legume seedlings, and growth of 4 species of rhizobia bacteria. Tests were carried out in a Bearden loam soil without previous record of insecticide application. Carbofuran was added at rates of 5, 50, and 500 ppm. Moisture-holding capacity was adjusted to 60%, and the treatments were incubated in 250 ml flasks capped with plastic film at 30°C.

Carbofuran had no effect on nitrification at any of the tested concentrations. Tested by the disc-inhibition method on a yeast-mannitol agar, carbofuran at 2 and 20 µl/disc had no effects on the growth of Rhizobium meliloti or R. japonicum, but there was some inhibiting effect on R. leguminosarum and R. trifolii.

The effect of carbofuran on the growth of legume seedlings was tested by growing sweet clover and alfalfa in disposable plastic pouches in 25 ml of nutrient solution to which carbofuran was added at 5, 50, and 500 ppm AI. After germination of the seeds, 1 ml of 1:5 (w/v) Nitragin AB, a preparation of nodulating bacteria, was distributed evenly over the seeds as an inoculum. Untreated control seeds were grown with and without inoculum. The plants were allowed to grow for 30 days under artificial light on a 12 hr on, 12 hr off photoperiod. The average dry weight of all plants was determined at the end of the 30-day period. The results in the carbofuran series, expressed as average dry weights of plants in milligrams, were as follows:

Carbofuran concentration	Alfalfa	Sweetclover
5 ppm	11.8	9.2
50 ppm	6.1	5.6
500 ppm	2.6	2.2
0 inoculated	12.6	7.9
0 noninoculated	6.0	5.6

This data indicates that, at the field use rate (5 ppm), carbofuran did not significantly affect the growth of the seedlings, while at 500 ppm, plant growth rates were well below those of both controls. Fifty ppm applications of carbofuran resulted in growth rates closely comparable to the noninoculated controls.

Hubbell et al. (1973) studied the effects of carbofuran and several other pesticides on the relative numbers of microbes and on nitrification in soil. The pesticides, alone and in combinations, had been applied to field plots at times and rates of application approximating agronomic practices in the growing of shadeleaf tobacco in the area of Quincy, Florida. The field plots were laid out on a Norfolk loamy fine sand prepared and fertilized for the growing of tobacco. Carbofuran was applied at the rate of 10 lb of AI/acre (11.2 kg/ha). Numbers of microorganisms and nitrification were monitored at 2-week intervals for 16 weeks following application.

The carbofuran treatments somewhat depressed the relative numbers of fungi, bacteria, actinomycetes and algae, although none of these effects were statistically significant at the 5% level. The rate of nitrification as determined by nitrate nitrogen appeared to be reduced by about 25% during the first 8 weeks in the carbofuran-treated plots, but the reduction was not statistically significant at the 5% level. In all treatments, there was a drastic reduction in nitrate nitrogen after 8 weeks. This reduction followed a heavy rainfall and was apparently due to leaching of the nitrate. There were no significant differences between treatments during the remainder of the experimental period.

Kulkarni et al. (1974) studied the effects of carbofuran and 3 other insecticides, applied to soil at their recommended rates, on the symbiosis of Rhizobium species with "groundnuts" (for example, peanuts), Arachis hypogaea. Carbofuran (type of formulation not given) at the rate of 16 kg/ha (14.2 lb/acre) was applied to red loamy soil of pH 6.8 in pots. (It is not clear whether the application rate is given in terms of active ingredient or formulated product.) Peanut seeds inoculated with a 5-day-old culture of Rhizobium species were sown in plots maintained under greenhouse conditions. Eight weeks after planting, some plants were removed carefully, and the number and fresh weight of root nodules were determined. The leghaemoglobin concentration of freshly excised nodules was determined. At harvest time, pot yield and dry matter weight of plants were recorded, and the nitrogen content of the plants was determined.

The carbofuran treatment had no significant effect on nodule numbers, but increased the fresh nodule weight in terms of milligrams per plant, and the average weight per nodule. Carbofuran had no significant effect on the leghaemoglobin content in the nodules, nor on the yield of peanut pods per plant, the dry matter weight, or the nitrogen content of the plant. The authors concluded that carbofuran, used at normal field rates, has no harmful effect on symbiotic nitrogen-fixing bacteria and peanut growth.

Harnish and Wendler (1972) conducted a study to determine the influence of carbofuran on the growth rate of 2 soil-borne fungi, Fusarium oxysporum f. lycoperisici and Pencillium digitatum. Carbofuran (5 ppm) was added to 25 ml of liquid broth medium in a sterile flask. The flasks were inoculated with a 4 mm block of agar plus mycelium and incubated on a gyratory shaker at room temperature. The mycelium and spores were harvested daily, washed, dried in a desiccator for 48 hr, and then weighed.

The P. digitatum grown in the carbofuran-treated medium produced a maximum amount of growth (208 mg) on the third day, whereas the untreated control reached a maximum (178 mg) on the second day. Conversely, F. oxysporum f. lycopersici grown in the medium containing 5 ppm carbofuran weighed 160 mg compared to 209 mg in the untreated control. The authors concluded that carbofuran slightly inhibits the growth of F. oxysporum f. lycopersici and slightly increased the dry weight of P. digitatum.

In another test, Harnish and Wendler (1972) studied the effects of carbofuran on microbial populations using a dilution plate technique. Soil was treated with 1,000 ppm AI carbofuran and then incubated at room temperature for 24 hr. The number of fungi on potato dextrose agar and the number of bacteria in nutrient agar were reported as follows:

Soil Treatment	Average Number of Microbes/g soil x 10^4	
	Bacteria[a/]	Fungi[b/]
Carbofuran 1,000 ppm	114	14
Untreated check	115	13

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a/ Isolated on nutrient agar

b/ On potato dextrose agar (PDA)

Counts per gram of treated soil did not differ significantly from the untreated check.

Chen et al. (1974) conducted a laboratory test to determine the effects of several organophosphate and carbamate insecticides on 2 commercial preparations of *Bacillus thuringiensis*. Carbofuran (75% wettable powder) was added to a thoroughly mixed suspension of *B. thuringiensis* at a concentration of 0.47 g AI/100 ml. The test surface, a sterile membrane filter of cellulose acetate, was inoculated with 0.2 ml of the test solution and allowed to incubate. Spore numbers on the filters were determined at 0, 2, and 4 weeks. Three replicates were used for each time interval.

Their results indicated that the addition of carbofuran to the commercial formulations of *B. thuringiensis* did not affect the survival of the bacteria on inert surfaces. Several of the insecticides tested, however, adversely affected the survival of *B. thuringiensis*.

Fauna - Thompson and Gore (1972) investigated the effects of carbofuran and a number of other insecticides on springtails, *Folsomia candida*, soil-inhabiting insects of the order Collembola that contribute to the breakdown of organic matter. To determine the direct contact toxicity of technical-grade carbofuran (95 to 99% purity), it was applied in a volume to volume ratio of 19:1 acetone: olive oil solvent mixture in a Potter spray tower. The spray was applied for 15 sec and 15 more sec were allowed for the droplets to settle. Because temperature can greatly affect the toxicity of insecticides, tests were run at 2 different pre treatment and post treatment temperatures, 13 and 24°C. The contact toxicity of carbofuran to *F. candida* was as follows:

Pre-treatment and post-treatment temperature (°C)	Average corrected % mortality caused by indicated % carbofuran solution			
	0.001	0.01	0.1	1.0
13	0	45	100	100
24	0	30	95	100

In further tests, Thompson and Gore (1972) determined the toxicity to springtails of carbofuran applied to a Plainfield sand that contained 6.5% water, 0.7% organic matter and, in the mineral fraction, 93.5% sand, 4.9% silt, and 1.7% clay. Carbofuran was applied to the soil in 9 different concentrations in chromatographically distilled *n*-pentane at 21 ± 2°C. Five g aliquots of treated soil were kept at 2 different pretreatment temperatures for at least 2 hr before 10 springtails per vial were placed on the treated soil. The test vials were kept in darkness for 24 hr before dead insects were counted. The following results were obtained with carbofuran in this test series:

Test temperature (°C)	Average corrected % mortality caused by indicated carbofuran concentration in soil (ppm dry weight soil)					
	0.005	0.01	0.05	0.1	0.5	1.0-50
13	5	5	5	35	100	100
24	0	0	20	95	100	100

This data shows that the direct contact toxicity of carbofuran to *F. candida* was not significantly affected by temperature. The carbofuran soil treatments were more toxic to the test insects at the higher temperature.

Kring (1969) studied the effects of carbofuran on the earthworm (*Lumbricus terrestris*). Carbofuran and the other materials were applied in the form of 10% granules in a band 20 cm wide over the row and raked in lightly. Shade tobacco was planted in the rows the day following the treatment. Dead and dying earthworms on the surface were observed and counted in the fields 6 days after the treatment. Only earthworms on the surface of the soil in the planted row were counted. Each plot consisted of a single row 6 m long, and the different treatments were randomized and replicated 4 times. The following numbers of dead earthworms were found in the carbofuran treatments:

Carbofuran rate kg/hectare = lb/acre (active ingredient)		Number of dead earthworms
0	0	0.25
0.56	0.5	8
1.12	1.0	12
2.24	2.0	20
4.48	4.0	20

Observations indicated that all earthworms in the immediate area of the carbofuran treatments at 2.0 and 4.0 lb/acre were killed. Blow flies (*Lucilia* species) attracted to the decaying earthworms were killed in large numbers in the plots treated with carbofuran.

Thompson (1971) and Thompson and Sans (1974) studied the effects of carbofuran and other insecticides on the numbers and biomass of earthworms (Lumbricidae) in pasture. The experiment was set up in a trefoil pasture that had not been treated with herbicides or insecticides for at least 5 yr. Carbofuran (from a wettable powder formulation) was applied at the rate of 4.48 kg of AI/ha (4.0 lb/acre) in a Latin square design to plots 10 ft square. Each treatment was replicated 10 times, and there were untreated strips 6 ft wide between plots and around the experimental area. Three weeks after treatment, the arithmetic mean of the number of earthworms found in 20 2 ft square wooden quadrats was 3.1 in the carbofuran-treated soil, compared to 17.9 in the untreated control, a reduction of 82.7%. In the carbofuran plots, the number of worms found in 20 quadrats ranged from 0 to 7, compared to 9 to 32 in the untreated control. The difference between the mean number of worms per quadrat between the carbofuran treatment and the untreated control was significant at $p > 0.01$. When earthworm counts were taken again 52 weeks after treatment, there were no statistically significant differences ($p = 0.05$) between numbers of earthworms in the carbofuran-treated and untreated plots.

The biomass of earthworms in the carbofuran-treated plots (in grams of fresh weight of the worms from 20 quadrats) 3 weeks after treatment was 160.3, compared to 404.6 in the untreated control, a reduction of 60.4%. The difference between the carbofuran-treated plots and the untreated control was significant at $p > 0.01$. There were no statistically significant differences in the mean earthworm biomass per quadrat between the carbofuran-treated and the untreated plots 52 weeks after treatment.

Chemical analysis of the earthworms obtained 3 weeks after treatment from the carbofuran-treated plots revealed no residues of carbofuran or its metabolites above the limits of detection of the analytical method. Samples were analyzed by gas chromatography, but the limits of detection for carbofuran were not given.

Stenersen et al. (1973 and 1974) studied the toxicity and mechanism of action of carbofuran in the earthworm (Lumbricus terrestris), and its metabolism by this species. Earthworms were obtained from a live bait dealer who had collected them largely from London, Ontario area golf courses, which would indicate that the worms had been exposed to many herbicides and insecticides. All worms used for experiments were sexually mature (showed well-developed clitella) and weighed between 3 and 5g. Worms were injected with dosages of carbofuran between 1.0 and 5.0 μg (0.5 to 1.55 mg/kg), and the LD_{50} was determined to be 1.3 mg/kg. When carbofuran was mixed in the soil (sterilized moistened loam; organic content approximately 20%, water content 10%, peat moss added at 1.5 by volume), the LC_{50} over a 5-day period was 12.2 ppm.

In in vitro cholinesterase studies of the inhibition of earthworm cholinesterase, the carbofuran concentration producing 50% enzyme inhibition was found to be $10^{-6.31}$ (0.5 ppm). Two organophosphates, tested under the same conditions, depressed earthworm cholinesterase more severely, while a methyl carbamate insecticide inhibited it less than carbofuran. Cholinesterase recovery in the live carbofuran-treated worms occurred more rapidly than in those treated with other chemicals tested. Characteristic signs of carbofuran poisoning were rigidity, immobility, sores and segmental swellings; only rigidity and immobility were observed after treatment with the organophosphorus insecticides.

In tests with ring-labeled ^{14}C carbofuran, it was determined that earthworms excreted carbofuran mainly as the unchanged parent compound, its hydroxylated analog (3-hydroxycarbofuran), and at least 2 unidentified products. The earthworms reabsorbed excreted insecticide and its metabolites from a sand medium. Earthworms excreted less than 10% of the total amount of carbofuran taken up originally. Comparing these observations with carbofuran metabolism studies on other organisms by other authors, Stenersen et al. (1973) concluded that the earthworm would appear to metabolize carbofuran initially in a similar fashion to both plants and other animals. They further suggested that the toxicity of carbofuran to earthworms may be caused by factors other than cholinesterase inhibition.

Gilman and Vardanis (1974) performed additional studies on the toxicity and metabolism of carbofuran in the common dew worm (L. terrestris), and a manure worm (Eisenia foetida), after seemingly conflicting reports on the effects of carbofuran on earthworms had been released by the manufacturer (FMC Corporation). Gilman and Vardanis discovered that the apparent discrepancy was not valid; FMC had used as its test animal a species that is not strictly an earthworm, i.e., E. foetida, a worm that inhabits animal dung and manure and feeds on organic debris without ever surfacing. By injection, carbofuran was about 6 times more toxic to L. terrestris than to E. foetida. When applied to the soil, carbofuran was twice as toxic to L. terrestris as to E. foetida.

When placed in soil treated with carbofuran at 4 ppm, coiling was always observed in both species. Eighty percent of the L. terrestris were found coiled at the soil surface within 24 hr while E. foetida showed some coiling, but remained buried in treated soils. In experiments designed to study the ability of the 2 species to detect carbofuran-treated soils, it was observed that carbofuran appeared to repel E. foetida but not L. terrestris. The authors pointed out that L. terrestris, which comprises a large percent of the detritus feeder biomass in Ontario, seems to be immobilized by carbofuran, as demonstrated by a marked inability to leave treated soils, leaving affected earthworms susceptible to predation and dehydration.

In uptake and excretion tests, the total amount of carbofuran taken up by both worms after 6 hr was similar when compared on the basis of micrograms per gram of worm. However, E. foetida excreted 95% of this material in 48 hr compared to only 10% excreted by L. terrestris. Approximately half of the material excreted by E. foetida was unchanged insecticide. Of the carbofuran metabolized by the worms in a 48-hr period, E. foetida retained only 5% as metabolites, whereas L. terrestris retained 87%.

The authors pointed out that this comparative study emphasizes that great care must be taken in selecting truly representative species for the evaluation of the ecological effects of chemicals.

Residues in Soil

Laboratory and Greenhouse Studies - Onsager and Rusk (1969) studied the residual toxicity of carbofuran and other insecticides to the sugar beet wireworm (Limonius californicus) in a laboratory experiment. Carbofuran 10% granules were applied at an initial concentration of 1.85 ppm, the field application rate suggested by the manufacturer. The insecticide was thoroughly incorporated into the soil ("Sagemoor sandy loam soil"). The treated soils were buried outdoors in specially prepared steel casings in such a manner that the level of soil inside the casing was flush with the level of the soil outside. The soils were kept moist by adding water to each casing twice each week. Soil samples were taken immediately after mixing and at 2, 4, and 6 weeks thereafter. All samples were subjected to bioassay with field-collected, sugar beet wireworms. The results observed in the carbofuran treatments were as follows:

Weeks after treatment	Percent mortality after indicated days of exposure				
	6-8	13-15	20-22	27-29	>41
0	30	56	74	100	
2	40	71	75	83	85
4	34	38			
6	36	83	91	95	

Chemical analysis of the carbofuran-treated soil showed that under the conditions of this test, carbofuran had an initial half-life of 36 days. About 20% of the initial concentration of carbofuran was still present in the soil 8 weeks after application.

Harris (1969b) employed a laboratory bioassay procedure to assess the persistence of biological activity of carbofuran and other insecticides in soils. Two soil types were used: Beverly fine sandy loam (pH 7.2, 1.5% organic matter, 76.6% sand, 21.1% clay), and a muck soil (pH 6.5; 64.6% organic matter; and 35.4% mineral content consisting of 14.5% sand, 38.8% silt, 46.7% clay). When treated with insecticide, the sandy loam contained 12.3 and the muck 164.0% water.

First-instar nymphs of the common field cricket, Acheta (Gryllus) pennsylvanicus, were used as test insects. The LD_{50} of carbofuran to this insect was 2.34 ppm in the sandy loam, 74.2 ppm in the muck soil. Equally large differences in toxicity between the 2 types of soil occurred for the other 9 insecticides investigated in the same manner. Soil persistence tests were run by applying carbofuran and the other insecticides to the 2 soils at levels of 4 times the LD_{50}. Samples were bioassayed at 0, 1, 2, 4, 7, 12, 16, 24, 36, and 48 weeks after treatment. In the sandy loam soil, the biological activity of carbofuran disappeared within 16 weeks, placing it into the "moderately residual" group ranging in between "highly residual" and "slightly residual" insecticides. In the muck soil, the biological activity of carbofuran persisted for about 24 weeks.

Campbell et al. (1971) studied the influence of organic matter content of soils on the efficacy of carbofuran and of several other insecticides on the wireworm, Melanotus communis, in the laboratory, following up on reports from the field about difficulties in controlling this insect. Carbofuran and the other insecticides were applied to Bladen silt loam soil (9.0% organic matter), organic loam soil (7.4% organic matter), and loamy fine sand (3.5% organic matter). Late-instar wireworm larvae collected from these soils in problem fields were placed in their respective native soils which had previously been treated with the test insecticides, including carbofuran from a 10% granular formulation at the rate of 1 and 2 lb AI/acre. Wireworm control of some of the other insecticides tested decreased with an increase in the organic matter content of the test soils, but carbofuran produced very low or no mortality of wireworms in any of the soils for reasons which the authors apparently did not investigate.

The persistence of the biological activity of carbofuran and 6 other insecticides in soil was studied by Thompson (1973), using Folsomia candida, a soil-inhabiting species of Collembola, as test insect. Equitoxic dosage rates of the test insecticides were thoroughly incorporated into Plainfield sand containing 6.5% water. The mineral fraction consisted of 93.5% sand, 4.9% silt, 1.7% clay, and there was 0.7% organic matter. For each insecticide, the application rate was the lowest concentration that would cause 100% mortality of F. candida in the soil in 24 hr, that is, 0.5 ppm in the case of carbofuran. Two parallel sets of the experiment were run at 2 different temperatures, 13 and 24 ± 1°C. Soil samples were bioassayed 1, 2, 4, 8, 12, and 16 weeks after treatment of the soils. Carbofuran killed 100% of the test insects at both temperatures throughout the entire test period. The author concluded that the concentration of carbofuran employed was too high, probably twice the LD_{99}, and that carbofuran did not degrade to less than the LD_{99} under the conditions of the experiment. Based on comparative data, the author classified carbofuran as "moderately persistent."

Getzin (1973) studied the persistence and degradation of ^{14}C-carbofuran in 4 different soil types under laboratory conditions. The physical and chemical properties of the 4 soils used were as follows:

Soil	Organic matter (%)	pH	Cation exchange capacity (meq/100 g)	Bulk density (g/cm^3)	Moisture equivalent (% of dry wt)	Clay (%)
Ritzville silt loam	1.0	7.8	17.8	1.2	20	19
Sultan silt loam	3.0	6.0	13.4	1.2	20	17
Chehalis clay loam	7.2	6.2	32.8	1.0	34	36
Organic (muck)	40.0	5.9	49.1	0.6	79	-

To determine the extent, if any, of microbial degradation, portions of these soils were radiation-sterilized. Initially, the irradiated soils were sterile, but they became contaminated with airborne spores during insecticide application and subsequent handling procedures. ^{14}C-carbonyl carbofuran was applied to irradiated and nonirradiated samples of the 4 soils at the rate of 20 µg/cm^3 and moisture levels were adjusted. Replicated samples of each soil were put into wide-mouth pint jars that were then equipped with CO_2 traps and kept in a constant-temperature room. Water was added periodically to maintain the moisture content within 5% of the original level. The NaOH in the CO_2 traps was replaced at 2- to 4-week intervals, and the absorbed CO_2 was precipitated and assayed for $^{14}CO_2$. Duplicate 20-cm^3 soil samples were removed for analysis at the desired intervals. Table 24 presents the results of this test in the 4 different soils at 0, 4, 8, 16 32, and 54 weeks after treatment. The parent compound, expired CO_2, and nonextractable residues in the soil accounted for most of the radioactivity. Water-soluble degradation products amounted to less than 1% of the extractable radioactivity in all soils throughout the experiment and are not included in Table 24. The data showed that the persistence of carbofuran varied considerably between soils; the approximate times required for 50% loss of carbofuran were about 4 weeks in the Ritzville silt loam, 8 weeks in the Chehalis clay loam, and more than 54 weeks in both the Sultan silt loam and the organic soil. Sterilization had no effect on the degradation rate of carbofuran in the Ritzville silt loam, and only a slight effect in the Sultan and organic soils, but significant effect in the Chehalis clay loam. Most of the ^{14}C from the degraded carbonyl-labeled carbofuran was expired as $^{14}CO_2$.

In a second test, Pitzville silt loam and Chehalis clay loam were treated with ^{14}C ring-labeled carbofuran at 5 µg/cm^3. The initial half-life of ring-labeled carbofuran in the 2 soils corresponded closely to the degradation rates for carbonyl-labeled carbofuran observed with these soils in the previous test. The breakdown of ring-labeled carbofuran resulted in the accumulation of nonextractable soil-bound radioactivity and a gradual evolution of $^{14}CO_2$. Only small quantities of carbofuran phenol, an expected degradation product of the insecticide, were recovered from treated soils.

When ^{14}C-carbofuran phenol was added to Ritzville silt loam and Chehalis clay loam at the rate of 5 µg/cm^3, the compound was bound to the soils very rapidly. Nonextractable radioactivity amounted to 21 and 24% in the 2 soils immediately after treatment, reaching a maximum of 70 to 80% of the applied rate 2 weeks after treatment. About 25% of the ^{14}C added as carbofuran phenol was expired as $^{14}CO_2$ within the 32-week experimental period. The soil-bound radioactivity and extractable radioactivity decreased gradually at the same time.

The persistence of carbofuran in relation to soil pH was determined in Sultan silt loam adjusted to 4 different pH levels and treated with carbonyl-^{14}C-carbofuran at the rate of 4 mg/400cm^3 of soil (10 µg/cm^3). Aliquot samples were removed at intervals and assayed. Carbofuran was rapidly degraded at pH 7.8; there was a tenfold difference in the time required for 50% breakdown between the soils at pH 4.3 and 7.8. This data indicates that the short residual life of carbofuran in the Ritzville silt loam (Table 24) was at least in part the result of alkaline degradation.

Table 24. Radioactive Carbofuran Equivalents Recovered as Carbofuran, Soil-Bound Residue, and Expired CO_2 from Irradiated and Nonirradiated Soils Treated with ^{14}C-Carbonyl-Labeled Insecticide at 20 µg/cm^3

Weeks after treatment	µg Equivalents/cm^3 of soil					
	Nonirradiated soil			Irradiated soil		
	Carbofuran	Soil-bound	CO_2	Carbofuran	Soil-bound	CO_2
			Ritzville silt loam			
0	18.7	0.1	0	18.2	0.2	0
4	10.0	0.8	7.1	10.8	1.8	3.3
8	5.5	0.9	10.2	6.0	3.1	5.3
16	2.4	0.7	13.9	2.2	3.4	6.8
32	0.9	1.3	15.6	0.9	3.6	10.6
54	0.4	0.9	15.8	0.4	3.2	11.0
			Chehalis clay loam			
0	19.3	0	0	19.2	0	0
4	13.5	0	7.3	18.4	0	0.5
8	9.2	0.1	9.8	17.6	0.2	0.8
16	5.5	0.4	11.9	15.5	0.3	2.1
32	3.6	0.3	14.4	14.0	0.7	5.2
54	2.5	0.2	15.7	11.1	1.1	9.4
			Sultan silt loam			
0	19.0	0	0	18.8	0	0
4	17.9	0	1.2	19.4	0	0.3
8	16.0	0.1	2.2	17.5	0.1	0.6
15	12.8	0.3	3.8	17.3	0.1	1.4
32	12.1	0.3	5.9	16.7	0.3	3.7
54	11.1	0.2	7.9	12.3	0.5	7.1
			Organic soil			
0	22.0	0	0	20.9	0	0
4	19.7	0	1.0	20.2	0	0.2
8	19.5	0.1	1.5	20.1	0.1	0.3
16	18.1	0.2	2.5	19.5	0.2	0.8
32	16.3	0.3	3.9	17.8	0.3	2.1
54	15.3	0.4	5.4	17.3	0.2	3.4

Source: Getzin (1973). Reprinted from Environmental Entomology by permission of the publisher.

Getzin (1973) concluded that rapid chemical hydrolysis is the primary route of degradation of carbofuran in alkaline soils. A slower breakdown occurs in acid and neutral soils, and is caused by both chemical and microbial degradation mechanisms.

Stanovick (1968) studied the degradation of carbofuran in 3 soil types (sandy loam, silt loam, and muck) treated with ^{14}C-ring- and carbonyl-labeled carbofuran at 2.0 and 9.0 ppm. Moisture content was maintained at 75% of field capacity in the sandy and silt loam soils, and 85% of field capacity in the muck soil. The soils were kept in wide-mouthed gallon jars at room temperature for 174 days. Fifty g samples were analyzed at various time intervals during the study period. The soil was exhaustively extracted with methanol, and the radioactivity in the extract was determined by liquid scintillation. Samples from the last time interval were (a) acid-hydrolyzed and extracted with methylene chloride, and (b) combusted by the Parr Bomb procedure.

The initial half-life of carbofuran under these conditions was 20 to 40 days. Carbofuran degraded fastest in the sandy loam and slowest in the muck soil; it dissipated 3.0 half-lives in the sandy loam, 2.3 half-lives in the silt loam, and 1.4 half-lives in the muck soil over the 174-day period.

Carbofuran was the only compound detected in the methanol and methylene chloride extracts by thin-layer and gas chromatography procedures. At the 174-day interval, the presence of 2,3-dihydro-7-hydroxy-2,2-dimethylbenzofuran residues was indicated in the Parr Bomb analysis, but this compound was not extractable from the soils by either methanol or acid hydrolysis. Acid hydrolysis, followed by methylene chloride extraction, was found to be the most efficient method for extraction of aged carbofuran residues.

Field and Combined Field/Laboratory Studies - Read (1969) studied the persistence of carbofuran and several other insecticides in acid mineral soils in the laboratory and in microplots in the field by a bioassay technique, using first-instar larvae of the cabbage maggot, *Hylemya brassicae*. Soils used in the field investigations were Kildare sandy soil (pH 5.2) and Charlottetown fine sandy loam (pH 6.4). The Kildare soil was also used in the greenhouse study. The tests were set up to simulate field conditions (banding 3/4 in deep in ridges) as closely as possible. Carbofuran was applied as a 10% granular formulation.

The activity of carbofuran in the field microplots, measured by percent mortality of *H. brassicae* larvae, was as follows:

Days after carbofuran application	Carbofuran concentration placed in the soil (ppm)			
	3	10	20	50
	Kildare sandy soil			
2	64	98	100	100
5	85	96	100	100
30	89	100	100	100
45	78	98	100	100
60	73	97	99	100
90	68	97	99	100
120	49	63	94	100
150	0	3	10	22

Days after carbofuran application	Carbofuran concentration placed in the soil (ppm)			
	3	10	20	50
	Charlottetown fine sandy loam			
2	98	100	100	100
5	98	99	99.9	100
30	90	96	99	100
45	97	99	100	100
60	88	93	100	100
90	91	90	100	100
120	0	0	8	32
150			4	12

Carbofuran, like most of the other insecticides studied, was more toxic to the larvae 3 to 5 days after application than within the first 24 to 48 hr. Reduction in toxicity occurred somewhat more slowly in the greenhouse than in the field. There was no marked difference in the rate of loss in toxicity in the sandy or fine sandy loam soils, indicating that the texture of the 2 mineral soils was not an important factor in toxicity degradation.

Read (1971a and 1971b) reported further observations on the activation, deactivation, bioactivity and persistence of carbofuran and several other insecticides in 2 other published articles. In the first of these (Read,1971a), field microplots were set up as described in the earlier studies (Read,1969, see above). The test insecticides were spread evenly 3/4 in below the soil surface at a rate equivalent to 100 ppm in the upper 1 in of soil. This concentration is somewhat higher than the recommended commercial rate of application for carbofuran in the area (60 to 70 ppm). At different time intervals after treatment, samples of the treated soils were taken to the laboratory, mixed thoroughly, and diluted serially with insecticide-free soil to obtain desired concentrations of toxicants in a given volume of soil.

Bioassays with first larval stages of the cabbage maggot, H. brassicae, demonstrated that carbofuran became biologically active soon after application. It was the most toxic of the compounds tested, and its toxicity persisted longer than that of several other insecticides tested at a given rate of toxicant per acre. At 30 ppm, carbofuran produced 100% mortality of H. brassicae larvae for at least 150 days; at 10 ppm, it remained 100% effective for about 80 days; at 3 ppm, close to 100% larval mortality was reached about 15 days after treatment, persisting for only about 15 days. At 1.5 ppm, maximum larval mortality (about 50%) occurred 15 days after treatment and declined gradually thereafter, approaching zero 80 days after treatment.

Carbofuran was the only insecticide in the group that showed readily detectable upward movement in the soil; flies resting on the surface of the carbofuran-treated soil were killed. In further studies of this observation, carbofuran was band-applied at different depths below the soil surface in ridged greenhouse microplots. The times required for toxicants of carbofuran to reach the soil surface were 1 week, 2 to 3 weeks, and 3 to 4 weeks, respectively, for the 1/2-, 3/4-, and 1 in depth of insecticide placement. In a second greenhouse test, dead flies were found on carbofuran-treated soil containing as low as 3 ppm of carbofuran.

Evidence that carbofuran toxicants actually moved into the surface soil was demonstrated by removing the upper ¼ in of soil and testing it for toxicity by the cabbage maggot bioassay method. At the field recommended rate for cabbage maggot control, sufficient toxic components of carbofuran moved from the 1 in depth of application into the upper 1/4 in of the soil to produce 100% mortality of test larvae after 3 to 4 weeks. When the upper 1/4 in of soil was transferred to a new area over untreated soil, toxicants could be detected by bioassay for 2 months. However, if left in the original microplots over the carbofuran-treated band, the upper layer of the soil remained toxic for at least 200 days. This observation indicates, according to Read (1971a), continual upward movement of toxic materials into the surface soil from the parent compound.

In the greenhouse trials, all toxic components of carbofuran decreased to nondetectable levels (below 0.5 ppm) within 300 days.

In another series of tests (Read, 1971b) on the bioactivity and persistence of insecticides against the cabbage maggot, H. brassicae, the performance of carbofuran essentially confirmed the author's previous findings. Among the insecticides included in this experiment, carbofuran was again the most toxic to the test organisms 30 days after application to field microplots at 100 ppm (in the manner described previously). Toxicity gradually declined in the carbofuran-treated soil, and toxic residues were barely detectable the following spring.

Hubbell et al. (1973), in studies on the microbiological effects of carbofuran and other pesticides described previously, also made observations on the persistence of the insecticides investigated. The test pesticides were applied to field plots at times and rates of application approximating agronomic practices in the growing of shadeleaf tobacco in northern Florida. Field plots were established on a Norfolk loamy fine sand prepared and fertilized as for a tobacco crop. Carbofuran was applied at the rate of 10 lb AI/acre (11.2 kg/ha). The carbofuran-treated soil was sampled 2, 4, 6, 8, and 10 weeks after application. Carbofuran was extracted from the soil samples and analyzed chemically. Carbofuran levels found were as follows:

Weeks after treatment	Carbofuran residue
2	0.95
4	0.90
6	1.25
8	1.05
10	0.55

Caro et al. (1973) studied the dissipation of soil-incorporated carbofuran in a 2-yr field investigation in two small watersheds at Coshocton, Ohio. Watershed No. 113 consisted of Keene and Rayne silt loam soil with an average pH of 6.35 and an average slope of 9.3%. Watershed No. 118 consisted of Coshocton silt loam, average pH 5.2 and average slope 9.6%. Both watersheds were plowed, disked, harrowed and fertilized in accordance with normal corn growing practices. Carbofuran 10% granules were applied broadcast at the rate of 4.83 lb AI/acre (5.41 kg/ha) to Watershed No. 113, followed within 30 min by disking into the 7.5 cm depth. Watershed No. 118 received carbofuran 10% granules at the rate of 3.71 lb AI/acre (4.16 kg/ha) applied in-furrow 5 cm deep in rows 1 m apart, along with the corn seed, without subsequent cultivation. The following year, in May of 1972, an in-furrow application of carbofuran 10% granules at the rate of 2.77 lb AI/acre (3.11 kg/ha) was made on Watershed No. 113. Watershed No. 118 was not retreated in 1972.

Soil samples were taken from numerous sampling points in each watershed on the day of carbofuran application and at 4 to 8 week intervals throughout both seasons. Carbofuran persistence in the soil, expressed in milligrams per square meter after each of the 3 treatments, is shown in Table 25. The disappearance curve in each case approximated a first-order reaction during the crop season. In 1971, half-lives were estimated to be 46 and 117 days in the broadcast and band applications, respectively. In 1972, the band application half-life was 94 days. Disappearance was slower during the cold months of the year. Despite the use of soil sampling techniques designed to minimize variation, variability in carbofuran content among samples and standard deviations were quite high. The irregularities parallel those found in similar experiments by the authors and by other investigators and are believed to be largely due to a lack of uniformity in pesticide field application.

Table 25. Carbofuran Residues in Soil Samples (mg/m^2)

Days after application	Range	Mean	Std. dev.	Range	Mean	Std. dev.
	Watershed No. 113 broadcast application, 1971			Watershed No. 118 band application, 1971		
0	215-726	404	126	365-1,508	775	353
29	146-588	265	102	376-1,558	743	362
63	65-244	147	50	375-920	575	157
113	17-140	69	33	126-633	343	143
153	9-129	46	31	142-551	311	126
225	4-97	30	25	28-558	203	126
337	8-59	22	14	51-134	76	28
	Band application, 1972					
0	628-1,046	830	177			
49	330-866	516	170			
89	224-665	392	167			
138	116-467	291	126			
160	135-537	306	159			

Source: Adapted from Caro et al. (1973).

As reported above, the 2 watersheds had soil pH values of 6.35 and 5.20, respectively. The half-life of pure carbofuran at these 2 pH levels in solution was determined to be 140 and 1,600 days, respectively. Thus, it is apparent that carbofuran decomposes more rapidly in soil, but it is not known whether chemical and/or biological mechanisms are responsible. The authors state that the observed differences in insecticide half-lives in the 2 watersheds were the result of differences in both soil pH and management practices.

Carbofuran residues disappeared much faster from certain small areas in each of the watersheds where the insecticide was banded. The residue values at these sampling points are not included in the data in Table 25 because these sites were obviously atypical. The factors causing this decreased persistence are not known, but moisture regime, soil pH, and physical structure of the soil are believed to be involved. The "rapid disappearance" areas were characterized by 1 or more of the following: greater runoff intensity; higher soil pH level (about 0.4 pH unit above that of the surrounding area); more clay-like soil texture; and soil moisture content that was higher by approximately 1.2% wet weight basis.

In an effort to further define the effect of temperature on the rate of decomposition of carbofuran, Caro et al. (1973) determined the activation energy of carbofuran hydrolysis and found it to be 38.5 kcal/mol. The mean soil temperatures during the season in Watershed No. 113 were 19.8°C in 1971 and 18.7° in 1972. Entering these values into the Arrhenius equation[a] indicates that the hydrolysis of carbofuran is a sensitive function of temperature, and that the half-life of carbofuran should have been about 50% longer in 1972 than in 1971. However, the actual half-life was more than twice as long (94 versus 46 days), suggesting overriding effects of other factors, especially placement. A substantial increase in persistence apparently occurred as a result of the band application.

Caro et al. (1973) also studied the losses of carbofuran in the runoff water from the treated watershed (see subsection on Environmental Transport Mechanisms, p. 129).

FMC Corporation (1974), in commenting on the studies by Caro et al. (1973) discussed above, points out that the observed dissipation rates of carbofuran in soils are not nearly as sensitive to changes in temperature and pH as the solution kinetic studies predict. From the Climatic Atlas of the United States, FMC calculated the mean temperatures during a typical growing season, June through September, for several areas. The Arrhenius equation was then used to predict the following relative half-lives for the hydrolysis of carbofuran in these areas during the summer months:

Area	Average temperature (°F)	Relative half-life
Caribou, Maine	60.3	1.000
Buffalo, New York	66.0	0.414
Lincoln, Nebraska	74.8	0.156
Amarillo, Texas	77.5	0.111
Memphis, Tennessee	79.0	0.092
Miami, Florida	81.5	0.056

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[a] $k = Ae^{E^*/RT}$

FMC analyzed the actual dissipation rates of carbofuran after broadcast application of 10% granules in a variety of soils from 6 states. The most rapid dissipation rate was only about 5 times greater than the slowest rate. No correlations between climate and dissipation rates were observed. A similar analysis of the dissipation of carbofuran after in-furrow application of 10% granules in soils from 8 states again showed no correlation between climate and dissipation rate. Again, there was approximately a 5-fold difference between the slowest and fastest dissipation rates.

The discrepancy between theoretical dissipation rates and those observed was considered to be due to several factors, including microbial action, insufficient moisture in the soil for true solution kinetics, catalysis of carbofuran decomposition by 1 or more soil constituent(s) and/or a complex reaction mechanism which does not conform to the Arrhenius equation. (The Arrhenius equation suggests that catalysis, i.e., lowering of the activation energy, would render the reaction less sensitive to temperature changes.)

FMC Corporation (1972a and 1974) conducted studies to evaluate the persistence of carbofuran in different soils following single applications, and the possible buildup of carbofuran residues in soil from repeated applications in successive years.

In 1 study, carbofuran residues were determined after single broadcast applications of carbofuran 10% granules in 6 different states, representing a variety of soils. The analytical results from different rates of application were normalized to a rate of 6 lb AI/acre. The average residues (in parts per million) found were as follows: 6.6 on day of application; 1.9 after 30 days; 0.31 after 75 days; 0.73 after 95 days; 0.21 after 130 days; 0.31 after 160 days; 0.06 after 360 days. The average variation ranged from 24 to 79% for sampling dates 0 to 130 days after application. There were no correlations between climate and dissipation rates.

The dissipation of carbofuran following in-furrow treatment with 10% granules was studied at 10 different sites in 8 states, again representing a variety of different soils. Analytical results were normalized to a rate of 1 lb AI/acre. Average residues (in ppm) found were as follows: 20 on the day of application; 12 after 40 days; 1.8 after 60 days; 0.52 after 150 days; 0.53 after 190 days; 0.13 after 360 days. The average variation ranged from 42 to 100%.

As other investigators have observed, this data indicates that carbofuran residues in the soil dissipate more rapidly following broadcast than following band treatment.

In a third set of studies, FMC Corporation (1974) evaluated carbofuran soil residues following repeated applications in successive years. The soils were planted with crops typical for each location. They were sampled twice each year, once in the fall at the time of harvest of the crop and once in the spring just prior to the next year's carbofuran application. This sampling schedule was followed for 4 yr, from the fall of 1970 through the fall of 1973.

There was no indication of an increase in soil residues following repeated applications of carbofuran in successive years. Treatments monitored included 5.0 (5 x 1.0) lb of 4 lb/gal flowable AI/acre/yr applied to potatoes in New York; 3 lb of 10% granules AI/acre/yr applied to corn in New York and Nebraska; 6 lb of 10% granules AI/acre/yr applied to tobacco in Arkansas; and 3 lb of 10% granules AI/acre/yr applied to peanuts in Arkansas. Carbofuran residues in the New York corn plots showed greater variations from year to year than those from Nebraska plots. This might be related to differences in method of application. Residues from tobacco plots receiving broadcast applications were fairly uniform from year to year.

Soil samples from these studies were analyzed by a method that included acid hydrolysis, methylene chloride extraction, Nuchar-atta clay column cleanup, and detection with a nitrogen-specific microcoulometric gas chromatograph. Carbofuran was the only carbamate compound detected above the method sensitivity of 0.10 ppm.

Residues in Water

The dissipation of carbofuran in flooded rice fields is summarized in a report by the FMC Corporation (1972a). In California, carbofuran residues in water were determined following postflood at the rate of 1 lb AI/acre: carbofuran residues in the water peaked at 0.7 ppm 8 hr after application. In another postflood test, maximum residues (0.3 ppm) were reached 14 hr after an application of carbofuran 2% granules at 0.5 lb AI/acre. When carbofuran granules were applied to rice fields preflood at the rate of 0.5 lb AI/acre, maximum residues in the water occurred 7 days after treatment, and these maxima were lower, for example, 0.1 ppm not tilled, and 0.05 ppm tilled.

Similar patterns were observed in tests in Louisiana rice fields. When carbofuran 2% granules were applied postflood at the rate of 0.5 lb AI/acre, carbofuran residues in the water peaked at 0.3 ppm 8 hr after treatment. Following a preflood application of carbofuran 3% granules at 0.5 lb AI/acre, maximum water residues, 0.2 ppm, were reached 2 days after application.

After peaking, carbofuran water residues dissipated with a half-life of 1 day or less. Residues reached nondetectable (0.01 ppm) levels within a few days. No other carbamate metabolites such as 3-hydroxy-carbofuran or 3-keto-carbofuran were detected.

Phytotoxicity

Tobacco plant responses to recommended and excessive rates of application of Furadan® 10G were studied by Tappin (1969). Furadan® 10G was broadcast by hand on February 25 at rates of 4, 6, and 10 lb AI/acre and roto-tilled to a depth of 6 to 8 in. Plots were bedded and transplanted 27 days later. An untreated check and a standard dust treatment were included in the randomized block, 4-replicate experiment. Plant response was evaluated by measuring the stalk height on the fifteenth and fifty-seventh day and by rating phytotoxicity on a scale of 0 to 4 weekly intervals from April 16 through June 25.

Plants responded well to Furadan®, as judged by plant height, but the 4 and 6 lb rates showed slight to moderate injury until early June. Plants treated at the 10 lb rate showed symptoms of severe phytotoxicity in May, but again had outgrown all effects by early June.

The author attaches little, if any, economic importance to the phytoxicity observed, especially at the 4 and 6 lb/acre rates. At proposed rates of application this has been limited to occasional chlorosis and, in unusually severe cases, small necrotic spots (flecks) on the lower leaves of the plant. Since these leaves are normally not harvested and usually drop prematurely due to lack of adequate sunlight, injury to these leaves is of no consequence. The improved growth of treated plants, particularly in the early season, more than offsets any possible early season injury to the unharvested older leaves.

Bioaccumulation and Biomagnification

The propensity of carbofuran for bioaccumulation and biomagnification was recently studied by investigators at the University of Illinois at Urbana-Champaign (Sangha,1972; Sanborn,1974; and Yu et al.,1974), using a laboratory terrestrial-aquatic model ecosystem developed by Metcalf et al. (1971). The model ecosystem consists of a terrestrial-aquatic interface and a 7-element food chain; it can be used to simulate the application of pesticides to crop plants and to study contamination of the aquatic environment. The system is housed in a glass aquarium (25 x 30 x 45 cm) and contains a sand-water interface consisting of 15 kg of sterilized white quartz sand and 7 liters of standard reference water.

Sorghum (*Sorghum halepense*) was grown in the sand for 7 days, followed by treatment with 5 mg (50 µCi) of ring-^{14}C- and carbonyl-^{14}C-labeled carbofuran in 0.5 ml of acetone (rate equivalent to 1 lb of carbofuran AI/acre). After treatment of the sorghum, larvae of the saltmarsh caterpillar, *Estigmene acrea*, were added to the system and allowed to feed on the treated sorghum plants; the larvae simulated the first member of a food chain, and acted as an effective distributing agent for the labeled pesticides within the system. The saltmarsh caterpillars died after they ate carbofuran-treated sorghum leaves. As a result, more caterpillars were added for the first 5 days after treatment until all sorghum leaves were consumed.

The water phase contained several members of a freshwater aquatic food chain, for example, frogs (species not identified), snails (*Physa* species), freshwater clams (*Corbicula manilensis*), freshwater crabs (*Uca minax*), water fleas (*Daphnia magna*), green filamentous algae (*Oedogonium cardiacum*), and a freshwater plant (*Elodea canadensis*). After 27 days, mosquito larvae were added to the system to become another member of the food chain, and after 3 more days, mosquito fish (*Gambusia affinis*) were added to become the final segment of the system. The experiment was carried out in 2 aquaria (tanks) each for ring-^{14}C- and carbonyl-^{14}-C-labeled carbofuran, respectively.

At the end of 33 days, the entire system was taken apart, and the organisms and water were extracted and analyzed for radioactivity. In addition, extracts were spotted on TLC plates, developed with appropriate solvents, and exposed to x-ray film to locate and identify the chemical composition of the solvent extracts. Metabolites were identified by co-chromatography with proposed metabolites, as well as by infrared, nuclear magnetic resonance, and mass spectrometry techniques.

At the end of the test period, none of the organisms contained residues of carbofuran. In the test with carbonyl-labeled carbofuran, several unknown compounds were isolated from *E. canadensis* along with 3-ketocarbofuran (35 ppb), N-hydroxymethyl carbofuran (35 ppb) and 3-hydroxy-carbofuran (11.8 ppb). Fewer metabolites were isolated from the experiment with ring-labeled carbofuran. As previously observed with 2 other carbamate insecticides, most of the carbofuran radioactivity was unextractable by acetone; values for ring- and carbonyl-labeled carbofuran were 69 and 77%, respectively. Small amounts of the unchanged carbonyl-labeled carbofuran (ca. 0.5 ppb) were isolated from the water phase of the system. Other metabolites found in identifiable quantities in the water portion were 3-ketocarbofuran, N-hydroxymethyl carbofuran, carbofuran phenol, and 3-hydroxycarbofuran, none of them in concentrations higher than 10 parts per trillion. It was concluded from these findings that carbofuran is highly biodegradable and has low residual activity in the components of the model ecosystem. Detoxification occurred by hydroxylation of the carbofuran molecule at several points. Metabolites were found only in the water phase (Sangha,1972).

Sanborn's conclusions from these studies on carbofuran and 2 other carbamate insecticides are as follows: "If the data obtained for these carbamates in this model ecosystem is representative of the behavior of aryl N-methyl carbamate insecticides, then it would appear that the use of these insecticides will not present ecological problems related to persistence and food chain accumulation" (Sanborn,1974).

Yu et al. (1974) provided additional details in regard to these carbofuran model ecosystem studies. His paper covers sample preparation and analytical techniques, and presents detailed, tabular data on the concentration of carbofuran metabolites and degradation products in solvent extracts and in residue fractions for ring-labeled and carbonyl-labeled carbofuran. The authors also report on the distribution of radioactive metabolites in solvent extracts after TLC analysis for both types of ^{14}C-carbofuran.

The radioactivity in the water was monitored throughout the experimental period. In both the ring- and carbonyl-labeled experiments, radioactivity in the water reached a peak on the seventh day. However, radioactivity in the tanks containing the ring-labeled carbofuran peaked at about 0.3 ppm, compared to less than 0.05 ppm in the tanks containing the carbonyl-labeled carbofuran. This indicated the rapid hydrolysis of carbofuran to carbofuran phenol and *n*-methyl-carbamic acid. The latter is then further degraded to CO_2 and other metabolites. To verify this conclusion, carbonyl-labeled carbofuran was placed in a closed aquatic system fitted with a CO_2 trap which contained NaOH. The radioactivity in the water decreased rapidly, while radioactivity in the CO_2 trap steadily increased. However, the radioactivity collected in the CO_2 trap was only about 25% of the total ^{14}C put into the system. The radioactivity remaining in the water was less than 10% of the introduced radioactivity. The authors explain this discrepancy in the ^{14}C balance by the inefficiency of the CO_2 trap.

As reported above, no parent carbofuran was found in any of the living organisms analyzed. However, large amounts of carbofuran were found in 2 crabs found dead the second day after applying carbonyl-labeled carbofuran to the tanks, and in 1 of the 2 crabs which became moribund after being introduced into the same tank 20 days after application. A second crab stocked in this tank at the same time did not die, and no intact carbofuran was found in this living crab at the end of the experiment on the thirtieth day. Apparently, the crabs did not metabolize carbofuran extensively as 61 to 92% of the radioactivity was extractable by acetone from the whole body. In other organisms, only about 20% of the radioactivity was acetone-extractable.

Insoluble residues remaining after acetone extraction from the water and organisms were not analyzed further and, therefore, their chemical nature is not known. The authors presume that they are conjugated with glucose or other large molecules because they are very polar.

In summarizing their findings, Yu et al. (1974) stated that carbofuran was rapidly hydrolyzed in water. Hydroxylation of the benzofuranyl moiety constituted the major degradation pathway.

Wong and Fisher (1975) determined the residues of carbofuran and its metabolites, 3-hydroxycarbofuran and 3-ketocarbofuran, in animal tissue by gas-liquid chromatography with electron capture detection as N-trifluroacetyl derivatives. The procedure has a minimum sensitivity of approximately 0.5 ppm carbofuran, 0.07 ppm 3-ketocarbofuran, and 0.05 ppm 3-hydroxycarbofuran for the test animals which were oyster, shrimp, mullet, menhaden, skate, and red-winged blackbird. After being fortified with 2.5 to 25.7 ppm carbofuran, 0.12 to 8.2 ppm 3-hydroxycarbofuran, and 0.23 to 0.82 ppm 3-ketocarbofuran, the resulting residues averaged 84.2, 83.8 and 72.8%, respectively.

Data on the rate of uptake and excretion of carbofuran by the common dew worm, *Lumbricus terrestris*, and a manure worm, *Eisenia foetida*, is reported in the subsection on Interactions with Lower Terrestrial Organisms, p. 109.

Other studies related to storage patterns of carbofuran and its metabolites in plants and animals can be found in the section on Metabolism and Metabolism in Mammals.

Environmental Transport Mechanisms

Lateral Movement - Bowling (1970) studied the lateral movement, sites of uptake, and retention of carbofuran applied in different ways to rice plants. Rice was planted in rows 20 cm long and 7.5 cm apart in metal trays kept under greenhouse conditions. The trays were fertilized 18 days after planting, then flooded to a water depth of 1 in. Twenty-one days after planting, the trays were moved to a growth chamber programmed to a 19 to 36°C daily temperature cycle and 14 hr daily illumination coinciding with the warmer period.

When the trays were placed in the growth chamber, carbofuran 3% sand-core granules were applied to the first 7.5 cm at one end of the tray at the rate of

1 lb AI/acre. Field-collected adult leafhoppers, Draeculacephala portola, were caged on each of the four rows of rice plants, and numbers of surviving leafhoppers were recorded at 6, 22, 24, and 48 hr after application of the carbofuran. The rate of survival of leafhoppers on the rice plants in relation to the distances of the plants from the center of the area where the carbofuran granules had been applied indicated that the insecticide moved laterally 22.5 cm in 22 hr in quantities toxic to the leafhoppers. Both carbofuran and its metabolites were absorbed and translocated by the plants, especially when carbofuran was placed near the roots prior to flooding, or when carbofuran wettable powder was placed on the leaf sheafs. The authors concluded that optimum utilization of carbofuran would be obtained by placement in dry soil, near the root system, followed by flood water.

Leaching Studies - FMC Corporation (1972a) studied the leaching properties of carbofuran in 7 different soil types in the laboratory, following the methods developed by Harris (1969a). In a segmented column consisting of aluminum tubing, soil was packed in 1-in segments to a height of 7 in, and ^{14}C-carbonyl-labeled carbofuran mixed with soil was placed in the second segment 1-in from the bottom. The column was then placed in a container in which water was kept at a constant level. Water moved upward in the column by capillary action to the soil surface when it was allowed to evaporate. After 3 days, each column segment was analyzed for radioactivity. The results showed that carbofuran moved more slowly in columns high in clay or organic matter. In soils of equal clay content, carbofuran moved further in soils with lower exchange capacity.

In this test, another pesticide was used as a standard, and its upward movement through comparable soil columns was monitored by bioassay. The rate of movement of carbofuran was slightly greater than that of the other pesticide, which Harris (1969a) classified as being "intermediate" in relative soil mobility.

Field leaching studies in 3 different soil types using lysimeters were conducted in Illinois. Carbofuran 10% granules were applied broadcast at the rate of 4 lb AI/acre over the top of lysimeters packed with Plainfield sand (little or no organic matter), Blount silt loam (light forest soil), and Elliot (an agricultural soil, highest among the 3 soils in organic matter). The lysimeters were embedded in a field exposed to normal year-round weather conditions.

Initial residues were 0.08 to 0.32 ppm in the runoff water and 0.005 to 0.009 ppm in the sediment. Some carbofuran residues percolated through the lysimeter containing the sandy soil. After 1 yr, negligible carbofuran residues were found in the top 1.5 ft of the 2 heavier soils; they were equally distributed throughout 3 ft in the sand. The lysimeters were new and had not fully settled at the start of the experiment. Therefore, the significance of the results is questionable.

The leaching behavior of carbofuran under field conditions was studied by analysis of soil samples from 2 corn fields in Iowa and Nebraska (treated with carbofuran 10% granules, at the rate of 1 lb AI/acre banded) and from 3 fallow fields in New York (treated with carbofuran 50% wettable powder at an exaggerated rate of 10 lb AI/acre broadcast). Maximum initial carbofuran residues in the corn field soils were 1.1 ppm. Residues below 6 in did not exceed 0.2 ppm during the entire growing season. In the samples from the fallow fields, initial residues of carbofuran were as high as 10 ppm in the upper 3 in soil layer. Residues of less than 0.1 ppm were found below 6 in over the year of sampling following treatment except for the muck soil. In all soil samples, essentially all carbofuran residues dissipated during the 1-yr sampling period.

In another study, a Nebraska fallow field and a Georgia tobacco field were treated broadcast with carbofuran 10% granules at the rate of 10 lb AI/acre. Samples from 0 to 6 in and 6 to 12 in depths were analyzed for carbofuran residues. The results were as follows:

Days after treatment	Nebraska fallow field		Georgia tobacco field	
	0-6 in	6-12 in	0-6 in	6-12 in
0	11.0	0.1	10.0	5.0
124	-	-	0.5	0.2
136	0.3	Nondetectable	-	-

The data shows that most of the carbofuran residue remained in the upper 6 in of the soil in both locations, and that the total residue decreased to less than 3% of the initial concentration in the Nebraska soil within 136 days and to 5% of the initial concentration in the Georgia soil within 24 days.

Runoff Studies - In the carbofuran dissipation studies discussed above (see subsection on Field and Combined Field/Laboratory Studies p. 120), Caro et al. (1973) investigated losses of carbofuran in the runoff water from both of the watersheds treated in 1971 and from the watershed that was retreated in 1972. The runoff-producing rainfalls and carbofuran losses in the runoff water are shown in Table 26. In 1971, the carbofuran losses occurred almost entirely in 2 heavy rains that fell within 48 hr after the application. In both watersheds, the carbofuran concentration in the runoff water was much higher in the second rainfall than in the first, indicating a greatly increased rate of release of carbofuran active ingredient from the applied granules by the second day.

In 1972, rainfall was more evenly distributed over the season, with measurable runoff occurring on the treated watershed on 13 occasions. Once again, the major carbofuran losses occurred in the early rainfall events. The first runoff-producing rainfall did not occur until almost 1 month after the carbofuran application. Therefore, the carbofuran concentrations in the runoff water never reached the high levels of 1971. The sudden increase in the carbofuran concentration that appeared 158, 173, and 179 days after treatment resulted from the disturbance of the soil surface at corn harvest which took place 154 days after application.

Some rainfalls were sufficiently intense to produce measurable quantities of carbofuran-bearing sediment in the runoff. Fine solids suspended in the water and coarser sediment deposited on the floor of the flume collecting the runoff were analyzed for carbofuran content. Residues on the suspended solids ranged from 0.46 to 1.64 mg/kg, and on the flume floor deposit from 0.98 to 1.11 ppm.

Table 26. Runoff-Producing Rainfalls and Carbofuran Losses in Runoff Water from Carbofuran-Treated Watersheds

Days after pesticide application	Amount of runoff (ℓ)	Average carbofuran concentration (μg/ℓ)	Carbofuran in runoff water (mg)
	Watershed No. 113 (broacast application), 1971		
1	31,900	473	15,089
2	7,170	1,394	9.995
39	1,480	537	795
65	120	33	4
82	300	15	5
239	3,760	5	19
Total	44,730		25,907
	Watershed No. 118 (band application), 1971		
1	40,640	272	11,054
2	3,470	1,002	3,477
239	9,190	19	175
Total	53,300		14,706
	Watershed No. 113 (band application), 1972		
26	35,840	191	6,845
28	61,320	223	13,674
53	30,710	58	1,781
76	630	8.8	6
82	3,190	6.9	22
91 (a.m.)	12,430	4.4	55
91 (p.m.)	9,170	2.9	27
119	1,130	2.8	3
123	6,160	1.8	11
147	2,710	2.6	7
168	11,400	14.2	162
173	33,970	16.9	574
179	34,020	19.9	677
Total	242,680		23,934

Source: Adapted from Caro et al. (1973)

In the 1972 runoff study, the concentration of 3-ketocarbofuran in the runoff water was also determined. About 5% of the parent compound was 3-ketocarbofuran. However, peak 3-ketocarbofuran concentrations were reached earlier in the runoff water than in the soil.

Overall, from 0.5 to 2.0% of the carbofuran applied was lost in runoff, most of it in water rather than in sediments.

Several additional carbofuran runoff studies have been reported by FMC Corporation (1972b). In Illinois, a 4-acre watershed close to a pond was planted with corn and treated with carbofuran 10% granules broadcast at the rate of 4 lb AI/acre. Soil, pond mud, and pond water samples were analyzed periodically. The initial half-life of carbofuran in the soil was 1 to 2 weeks on the average of 7 sampling stations, varying somewhat in relation to soil pH. Initial soil residues of about 1 ppm reached levels of less than 0.1 ppn by the fall and were nondetectable the following spring. Residues of about 1 ppm occurred in the pond water following a heavy rainfall 4 days after treatment. This residue declined to "negligible" by the next sampling date (16 days from application and 12 days from first sampling), and was not detectable thereafter. Highest residues of 0.2 ppm were found in the pond mud during the first few weeks after the runoff, but they disappeared thereafter. There was no fish mortality in the pond.

In another runoff study, carbofuran 10% granules were applied broadcast at the rate of 6 lb AI/acre to the top 4 ft strip of 24 ft x 24 ft plot having a 4% slope. Soil cores of 6 in were taken at 1 ft intervals in 3 replicates downslope, starting in the treated zone, down to 3 water-catch basins at the base. Soil samples were taken periodically throughout the growing season, and water samples were taken from the catch basins after each significant rainfall. In the treated zone, carbofuran residues declined to 10% of the initial concentration within 64 days. Residues were found in the first foot below the treated zone, but none further downslope. No detectable residues (0.01 to 0.02 ppm detectability) were found at any time in runoff water collected in the catch basins 25 ft downslope.

In western Iowa, 4 watersheds (2 to 4 acres in size with slopes of 15 to 20%, containing alluvial silt with about 2% organic matter content) were treated with carbofuran 10% granules banded on corn at planting time at the rate of 1 lb AI/acre. Runoff water and sediment were collected through flumes and waterwheels. Three major rainfall events created measurable runoff on one or more of the watersheds 37, 60, and 70 days after planting. Analysis of the runoff showed carbofuran residues of 0.15 ppm or less in the water and 0.7 ppm or less in the sediment. There were no significant differences in carbofuran residue content between the watersheds. There was less runoff of water and sediment from ridge-planted than contour-planted watersheds.

In California, an 8.5 acre tomato field (sandy loam, average pH 8.2) was sprayed by air with a concentration of carbofuran 4 lb AI/gal (flowable formulation) applied at the rate of 1 lb AI/acre. At the time of treatment the tomato plants provided a canopy that protected from one-third to two-thirds of the soil surface from the direct spray. The treated field was furrow-irrigated weekly for 4 weeks. Soil samples were taken at weekly intervals from 3 points: (a) along the plant beds not covered by the plant canopy (exposed bed); (b) along the plant rows in the area protected from the spray by the foliage (protected row); and (c) in the irrigated furrows that were also exposed to the direct spray. Soil samples were taken to a 6 in depth, with 25 cores diagonally across the field comprising one sample. Duplicate samples were taken along the other diagonal.

Carbofuran residues in the exposed bed (a) declined from a maximum of 0.3 ppm 4 days after application to below 0.05 ppm after 32 days. Residues in the protected row (b) slowly increased to a maximum of 0.09 ppm within 25 days, then declined to 0.01 ppm at 32 days. Residues in the exposed irrigation furrow (c) declined from 0.3 ppm at the day of treatment to below 0.05 ppm 24 days after treatment.

Samples of the irrigation water (pH 8 to 9) were taken several times during each irrigation along the tail ditch draining the field at distances of 0, 750, and 1,500 ft along the ditch. Maximum carbofuran residues of 0.1 ppm were found at the head of the ditch 1 day after spraying. Residues decreased with distance along the ditch and declined to undetectable levels (less than 0.0023 ppm) throughout the entire length of the ditch within 28 days after treatment.

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PART II. INITIAL SCIENTIFIC REVIEW

SUBPART D. PRODUCTION AND USE

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This section contains data on registration and on production and uses of carbofuran. The section summarizes rather than interprets scientific data reviewed.

Registered Uses of Carbofuran

Federally Registered Uses - Carbofuran is a broad spectrum insecticide-nematicide registered as a contact insecticide on crops and as a systemic soil treatment. The chemical was introduced for commercial use in agriculture in the United States about 1970. Carbofuran has been highly effective against corn rootworms and alfalfa weevils. Dosages, tolerances and limitations for currently registered uses are summarized in Table 27.

Production and Domestic Supply

Volume of Production - Carbofuran is produced in the United States by a single manufacturer, the Agricultural Chemical Division of FMC Corporation, Middleport, New York.

The United States Tariff Commission (1973b, 1974) does not report the production and sales volumes of carbofuran individually. Carbofuran is included in the category "All Other Cyclic Insecticides and Rodenticides."

In comparison to all other pesticides in this category, the production and sales volumes of carbofuran are so small that Tariff Commission data is not significant in estimating carbofuran volumes. However, carbofuran was one of 25 selected pesticides whose production, distribution, use, and environmental impact potential was studied by von Rumker et al. (1974). Estimates for 1972 placed domestic production of carbofuran at 6.0 million lb.

Imports - A report by the U.S. Tariff Commission (1973a) shows an absence of carbofuran imports. The probability that there were no imports of carbofuran into the United States in 1972 is further supported by the fact that the product is the subject of a patent held by the only U.S. producer, FMC Corporation.

Exports - Carbofuran is not listed in the U.S. Bureau of the Census commodity descriptions on pesticide exports for 1970 (U.S. Bureau of the Census, 1971). This may be due to the fact that, at least in some statistics, carbofuran is classified as a nematicide. The reports do not contain a separate breakdown of nematicides.

However, von Rumker et al. (1974) estimated that, in 1972, approximately 1.0 million lb of carbofuran AI were exported from the United States.

There are indications that the export volume of carbofuran is increasing. Carbofuran is an effective, versatile insecticide and nematicide that is in demand in other parts of the world. According to von Rumker et al. (1974), recent increases in carbofuran production capacity have eased supply problems that limited carbofuran export (as well as domestic) sales in the early 1970's. It is considered likely that not only domestic (see below) but also export sales of carbofuran have increased since 1972.

Domestic Supply - As estimated by von Rumker et al. (1974), approximately 5.0 million lb of carbofuran AI were used in the United States.

Formulations - Carbofuran is not available domestically as technical active ingredient. The only formulations available are those from the basic producer, the Agricultural Chemical Division of FMC Corporation. FMC currently offers 4 different carbofuran granular formulations containing, respectively, 10, 5, 3, and 2% AI. In addition, a flowable formulation containing 4 lb is available. These formulations are marketed under the trade name Furadan®. Furadan® 2, 3, and 10% granules, and 4 lb/gal flowable formulation produced by FMC are also marketed by the Chemagro Division of Mobay Chemical Corporation, Kansas City, Missouri. Most or all of the carbofuran granular formulations are dense, freeflowing, uniform sand-core granules. Accurate calibration of application equipment is essential to distribution of carbofuran at the intended dosage rate.

Use Patterns of Carbofuran in the United States

General - Carbofuran is an insecticide-nematicide with a broad spectrum of biological activity. It can be used either as a contact insecticide applied to the foliage of target crops, or as a soil-applied systemic insecticide-nematicide. Applied to the soil, carbofuran controls certain soil-inhabiting pests. In addition, it is systemically absorbed by the roots and translocated by treated plants to provide control of a number of foliar pests. It is the most effective insecticide currently available against corn rootworms and especially against some strains that are resistant to other insecticides.

Carbofuran is registered, recommended and used in the United States primarily on certain agricultural crops, as outlined in greater detail in the preceding section. There are only a few nonagricultural uses, namely, application as a soil treatment to cottonwoods and Siberian elms, and as a clay slurry for the treatment of pine seedlings. These nonagricultural uses account for only very small quantities of carbofuran active ingredient. The product is not registered or used for any other industrial, commercial, or institutional pest control purposes, nor for use on ornamentals, in home gardens or indoors. Thus, most of the quantities of carbofuran currently used in the United States are agricultural.

Carbofuran was introduced in the U.S. for commercial agricultural use in about 1970. Its use increased rapidly, mainly due to its superior effectiveness against corn rootworms and alfalfa weevils. These insects were major economic problems, becoming resistant to certain other insecticides when carbofuran became available and placing it in great demand.

Carbofuran Uses in 1971 - Carbofuran is reported individually in the U.S. Department of Agriculture's survey of the quantities of pesticides used by farmers in 1971 (U.S. Department of Agriculture, 1974). Table 28 summarizes the uses of carbofuran in the United States. Uses are shown both by quantities of carbofuran AI and by numbers of acres treated. According to the U.S. Department of Agriculture's survey, 93.9% of the total quantity of carbofuran used by farmers in 1971 was used on corn, followed by rice (5.7%). Other field crops, vegetables and fruit and nut crops accounted for the balance (0.4%). The U.S. Department of Agriculture's data indicates that carbofuran was used at an average rate of 0.73 lb AI/acre on corn whereas the average use rate on rice was 2.1 lb AI/acre. The latter rate is questionable, however, since it exceeds recommended rates. As indicated in the section on Carbofuran Uses in California, there is approximately a 12-fold discrepancy between the USDA and California data on usage for rice.

Table 29 summarizes the use of carbofuran in the U.S. in 1971 by regions, by quantity used, and by acreage treated. This data indicates that about 90% of the total quantities of carbofuran used in 1971 were used on corn in the corn belt, lake and northern plains states. In the Pacific and delta states, carbofuran was used primarily on rice. The remaining quantities of carbofuran used by farmers in 1971, according to the USDA survey, were used primarily on corn in the northeastern, mountain, and Appalachian states.

Carbofuran Uses in 1972 - In 1973 and early 1974, von Rumker et al. (1974) conducted a comprehensive study on the production, distribution, use and environmental impact potential of 25 selected pesticides, including carbofuran. They estimated that, in 1972, 5.0 million lb of carbofuran AI were used on agricultural crops in the United States. Of this total, an estimated 4.4 million lb were used in the north central states, 200,000 lb each in the south central and western states, and 100,000 lb each in the northeastern and southeastern states. The authors' surveys further indicated that, in 1972, uses of carbofuran for industrial, commercial, institutional, governmental, or home garden pest control purposes were negligible, if used at all.

Figure 8 presents the materials flow diagram for carbofuran for 1972 from the report by von Rumker et al. (1974). This figure shows the flow of raw materials (open arrows) to FMC's plant in Baltimore, Maryland, where 2,3-dihydro-2,2-dimethyl-7-benzofuranol, the final intermediate in the production of carbofuran, was produced in 1972. This intermediate was then transported to another FMC plant in Middleport, New York, where the final reaction step and the formulation of the technical active ingredient were carried out. Shaded arrows, graduated in proportion to the quantities represented, indicate the flow of carbofuran products to the major use areas. Where substantial quantities of carbofuran were used in 1972, the geographic distribution is broken down by states or small groups of states (boundaries indicated by light shading of the state lines). Smaller uses in larger geographic areas are broken down to the level of the regions whose boundaries are indentified by dark shading of the state lines concerned.

Carbofuran Uses in 1974 - Von Rumker et al. (1975) studied the use of soil insecticides on corn in 1974 in 8 midwestern states (Iowa, Illinois, Indiana, Ohio, Missouri, Minnesota, South Dakota, and Nebraska). These 8 states accounted for 75% of the total acreage of corn grown for grain in the United States in 1974. It was concluded from a survey of extension entomologists and of pesticide trade sources in these states that, in 1974, approximately 5.3 million lb of carbofuran active ingredient were used on corn in the 8 states surveyed. Taking into account this information and the state use patterns of carbofuran as reported by the U.S. Department of Agriculture (1974) for 1971, it is estimated that, in 1974, approximately 6.8 million lb of carbofuran active ingredient were used on corn in the U.S. (6.3 million lb in the corn belt, lake and northern plains states, 500,000 lb in the remaining corn growing states).

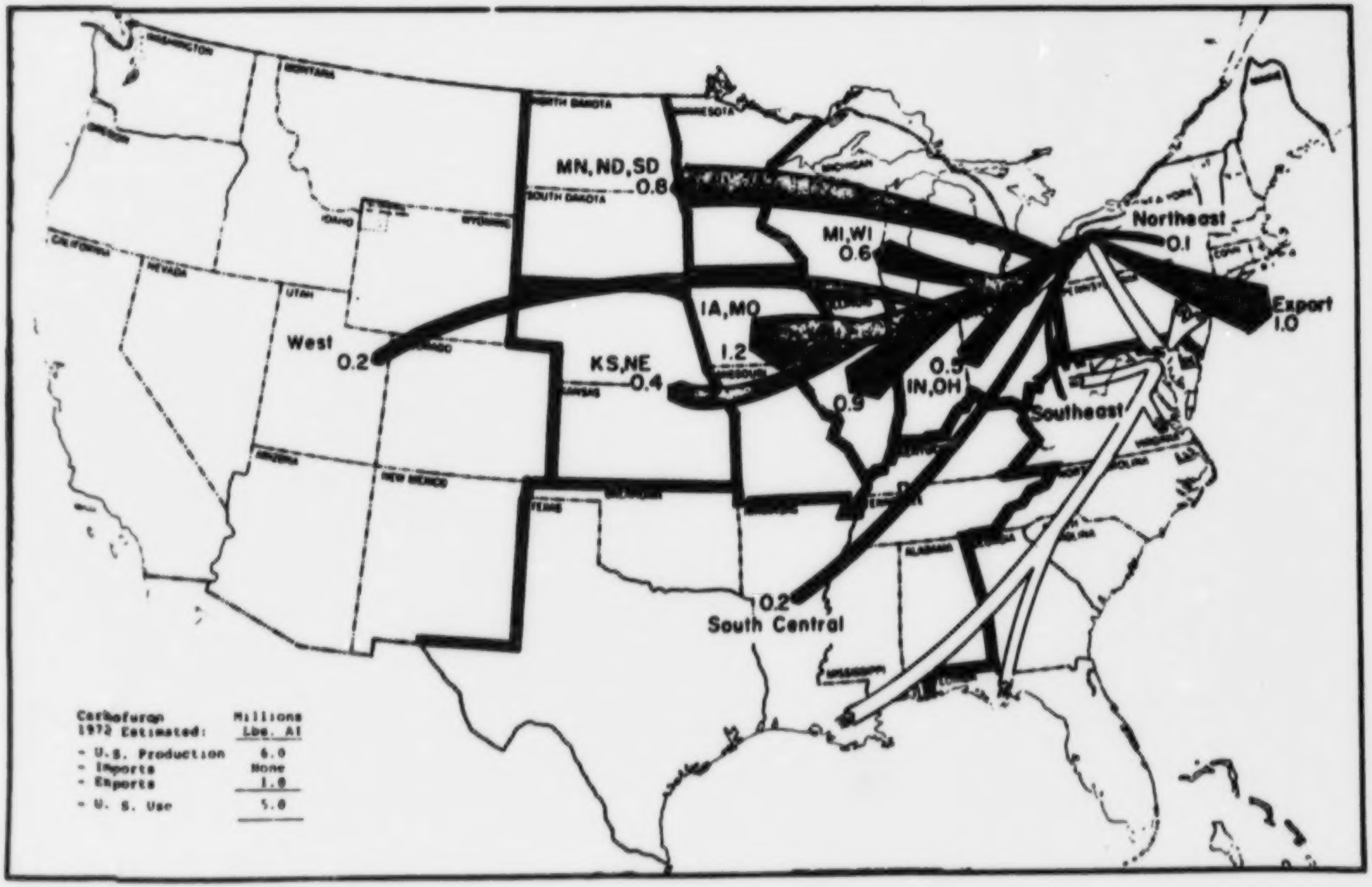
Carbofuran Uses in California - The California Department of Food and Agriculture keeps detailed records of pesticide uses by crops and other uses; the data is published quarterly and summarized annually. Table 30 summarizes the uses of carbofuran in California by major crops for the 1970 - 1974 period. According to the California reports, the annual volume of carbofuran used in the state increased from 9,500 lb AI in 1970 and 1971 to 10,600 lb in 1972, 106,000 lb in 1973, and 146,000 lb in 1974.

During the 5-year period covered by Table 30, the quantities of carbofuran used on rice in California ranged from a low of 7,800 lb in 1972 to a high of 11,300 lb in 1973. The use of carbofuran on alfalfa increased rapidly, from 100 lb AI in 1971 to 2,700 lb in 1972, 94,000 lb in 1973, and 135,700 lb in 1974. There were no significant uses of carbofuran on other crops during this period, according to the Department of Food and Agriculture's reports. It should be noted there is a large unexplained discrepancy between the quantities of carbofuran used on rice in California in 1971 according to the California Department of Food and Agriculture--8,700 lb, and that reported by the U.S. Department of Agriculture (1974)--103,000 lb.

Table 31 presents the carbofuran uses in California by crops and other uses, number of applications, pounds of active ingredient, and number of acres treated for 1972, 1973, and 1974, the 3 most recent years for which such data are available.

Table 32 summarizes the estimated uses of carbofuran in the United States by regions in 1971, 1972, and 1974, based on reports, estimates and information sources discussed in the preceding subsections of this chapter. It is emphasized that the estimates for 1971 are those reported by the USDA (1974), whereas those for 1972 and 1974 were obtained by RvR Consultants. The RvR data estimates for these 2 yr are not directly comparable to those for 1971 from USDA since sources and methods are different. RvR's 1972 and 1974 surveys as well as pesticide use reports from several of the north central states suggest that USDA's reported total use of carbofuran in 1971, 2,860,000 lb, may be low. It is believed that the use of carbofuran in the United States did not actually increase by about 75% (from 2.86 to 5.0 million lb) from 1971 to 1972, but that the actual use volume in 1971 was somewhat higher than estimated by USDA and that, accordingly, the rate of growth from 1971 to 1972 was not quite as steep.

It is estimated that in 1974 7.2 million lb of carbofuran active ingredient were used in the United States. Of this total, 6.3 million lb (88%) were used in the north central states, primarily on corn. An estimated 400,000 lb were used in the western states primarily on alfalfa and rice. About 250,000 lb were used in the south central states, mainly on rice. The remaining 250,000 lb were used in the northeastern and southeastern states, mainly on corn.



Source: von Rumker et al. (1974).

Figure 8. Materials Flow Diagram for Carbofuran (1972)

Table 27. Currently Registered Uses of Carbofuran

Site and pest	Dosage (lb actual)	Tolerance, use, limitations
Agricultural crops		
Alfalfa		10 ppm (fresh alfalfa) (not more than 5 ppm carbamates). 40 ppm (alfalfa hay) (not more than 20 ppm carbamates). 7-Day preharvest interval through 0.25 lb/acre. Foliage application. 14-Day preharvest interval above 0.25 through 0.5 lb/acre. Foliage application. 28-Day preharvest interval from above 0.5 through 1.0 lb/acre. Foliage application. Do not apply more than once per season. Apply only to pure stands of alfalfa. Do not move bees into alfalfa fields within 7 days of application.
Alfalfa blotch leaf miner	1.0/acre (flow)	Northeastern states. Apply when insects appear.
Alfalfa snout beetle	0.25-1.0/acre (flow)	Use restricted to New York state. Foliage application. Apply when insects appear or feeding is first noticed.
Alfalfa weevil (larvae)	0.25-1.0/acre (WP, flow)	Foliage application. Apply when larval feeding is first noticed.
Alfalfa weevil (adults)	0.5-1.0/acre (flow)	Foliage application. Apply when adults appear.
Egyptian alfalfa weevil (larvae)	0.25-1.0/acre (WP, flow)	Foliage application. Apply when larval feeding is first noticed.
Grasshoppers	0.125-0.25/acre (flow)	Use when grasshopper feeding is noticed.
Lygus bugs	1.0/acre (flow)	Foliage application. Apply prior to bloom.
Pea aphid	0.25-1.0 acre (flow)	Foliage application. Apply when insects appear.
Potato leafhopper	1.0/acre (flow)	Apply when insects appear.
Bananas		0.1 ppm. No preharvest interval through 3.0 lb/acre or 5.5 g/unit of production (cepa). For export to Central and South America.
Banana root borer	1.25-1.5 g/cepa (G)	At planting time treatment. Apply 0.8-1.0 g to planting hole and 0.45-0.5 g to the soil surface after the hole has been filled in. -plus-
	2.0 g/cepa (G)	Soil treatment. Apply 4 months and again 8 months after planting.
	2.0-2.5 g/cepa (G)	Soil treatment to established plantings. Apply twice per year. For the first treatment apply 0.4-0.5 g around the base of the mother, daughter and granddaughter plants. For the second treatment apply 1.6-2.0 g over an area of 50 cm around the producing unit including the mother, daughter and granddaughter plants.
Corn (field)		0.2 ppm (grain) (not more than 0.1 ppm carbamates). 25 ppm (fodder and forage) (not more than 5 ppm carbamates). Multiple applications allowed if 1.0lb or less was used at planting.

Source: U.S. Environmental Protection Agency, EPA Compendium of Registered Pesticides, Vol. III (1974).

Table 27. (Continued)

Site and pest	Dosage (lb actual)	Tolerance, use, limitations
Corn (continued)		
Armyworm Armyworm, fall	0.75-1.0/acre (with 40-in. row spacing) or 0.75-1.0/13,000 linear feet of row (G)	(1) Direct granules into planter shoe with seed or (2) place applicator into furrow and mix with the covering soil or (3) apply granules in 7-in. band behind planter shoe and incorporate into top inch of soil. Will control armyworm and fall armyworm for approximately 4-6 weeks.
Corn borer, European Second and third generations	0.75-1.0/acre (with 40-in. row spacing) or 0.75-1.0/13,000 linear feet of row (G)	Soil treatment at time of planting. Apply in a 7-in. band over the covered seed row. Incorporate into top inch of soil. Claims are limited to aid in the control of first generation European corn borers.
	1.0/acre (G)	Foliage application. Broadcast by air or direct granules into whorls with ground equipment. Apply when eggs begin to hatch. Do not make over two foliage applications per season.
First generation	2.0-3.0/13,000 linear feet of row (with 40-in. row spacing) (G)	For control of first generation larvae. (1) Direct granules into planter shoe with seed or (2) place applicator into furrow and mix with the covering soil or (3) apply granules in 7-in. band behind planter shoe and incorporate into top inch of soil.
Corn borer, southwestern	1.0/acre (G)	Foliage application. Broadcast by air or direct granules into whorls with ground equipment. Apply when eggs begin to hatch. Claims limited to control of second and third generation larvae. Do not make foliage application if more than 1.0 lb actual carbofuran was applied at planting. Do not make over two foliage applications per season.
	1.5-3.0/acre (with 40-in. row spacing) or 1.5-3.0/13,000 linear feet of row (G)	Apply in the seed furrow at time of planting.
Flea beetles	0.75-1.0/acre (with 40-in. row spacing) or 0.75-1.0/13,000 linear feet of row (G)	(1) Direct granules into planter shoe with seed or (2) place applicator into furrow and mix with the covering soil or (3) apply granules in 7-in. band behind planter shoe and incorporate into top inch of soil.
Nematodes (dagger, lance, lesion, root-knot, spiral, sting, stubby root, stunt)	1.5-2.0/13,000 linear feet of row	Apply at planting time in a 7-15 in. band and incorporate into the top 3 in. of soil.
Rootworms, corn	**0.75-1.0/acre (with 40-in. row spacing) or 0.75-1.0/13,000 linear feet of row (flow, G)**	Apply susp. in a 7-in. band over the row, or inject it on each side of the row. Susp. may be mixed with liquid fertilizer. Be certain mixture is physically compatible. Do not mix until ready to use. Apply G into the seed furrow at time of planting.

Table 27 (Continued)

Site and pest	Dosage (lb actual)	Tolerance, use, limitations
Corn (field) (Continued)		
Rootworm, northern corn	0.75-1.0/acre (with 40-in. row spacing) or	Soil treatment at time of planting. Apply in a 7-in. band over the covered seed row. Incorporate into the top inch of soil.
Rootworm, southern corn	0.75-1.0/13,000 linear feet of row (G)	Postplant soil treatment. Apply by banding over the row and incorporate it into the soil, or by side-dressing on both sides of the row.
Rootworm, western corn	0.75-1.0/acre (with 40-in. row spacing) or 0.75-1.0/13,000 linear feet of row (G)	Soil treatment at time of planting. Apply in a 7-in. band over the covered seed row. Incorporate into the top inch of soil.
Stalk rot	0.75-1.0/13,000 linear feet of row (G)	Apply a 7-in. band and incorporate into the top 1-in. of soil. This treatment reduces losses due to stalk rot by reducing the incidence of insect wounds which permit entry of the stalk rot fungus.
Wireworms	2.0-3.0/acre (with 40-in. row spacing) or 2.0-3.0/13,000 linear feet of row (G)	Soil treatment at time of planting. Apply in a covered band or in the seed furrow.
Peanuts		0.2 ppm (not more than 0.1 ppm carbamates) (peanuts). 5 ppm (not more than 1 ppm carbamates) (peanut hulls). Do not feed treated forage to dairy animals or animals being finished for slaughter.
Thrips	2.0-4.0/acre (with 36-in. row spacing) or 0.133-0.275/1,000 linear feet of row (G)	Use restricted to Southeastern states. Apply in 12-in. band over the row prior to planting. Incorporate into top 3-6 in. of soil.
	3.0-5.0/acre (with 36-in. row spacing) or 0.2-0.35/1,000 linear feet of row (G)	Use restricted to Southeastern states. Apply in 18-in. band over the row prior to planting. Incorporate into top 3-6 in. of soil.
Nematodes (lesion, ring, root-knot, sting, stunt)	2.0-4.0/14,520 linear feet of row	Use restricted to Oklahoma, Texas and southeastern states. Apply as a 12-in. band over the row and incorporate into the top 3-6 in. prior to planting.
Potatoe leaf hopper	0.033-0.066/1,000 linear feet of row	Use restricted to south-eastern states. Apply in seed furrow at time of planting.
Rootworm, southern corn Thrips	0.5-1.0/acre (with 36-in. row spacing) or 0.033-0.066/1,000 linear feet of row (G)	Use restricted to southeastern states. Apply in the seed furrow at planting. This treatment will also aid in controlling southern corn rootworms.
Peppers		1.0 ppm (not more than 0.1 ppm carbamates). 21-Day preharvest interval through 3.0 lb/acre. Side-dress soil application.

Table 27. (Continued)

Site and pest	Dosage (lb actual)	Tolerance, use, limitations
Peppers (continued)		
European corn borer	2.0 and 3.0/acre (with 38-in. row spacing) or 0.075 and 0.1/500 linear feet of row (G)	Side-dress soil treatment to one or both sides of the row. If application is made to both sides, use half the specified row dosage per side. Make two applications. Apply low dosage 2-4 weeks after transplanting and high dosage 4-6 weeks later. Incorporate into soil.
Green peach aphid	2.0 and 3.0/acre (with 38-in. row spacing) or 0.075 and 0.1/500 linear feet of row (G)	Use restricted to the Delmarva Penninsula and southern New Jersey. Side-dress soil treatment to one or both sides of row. Make first application 2-4 weeks after transplanting. Make second application 4-6 weeks later.
Potatoes		2.0 ppm of which no more than 0.1 ppm is carbamates.
Aphids Colorado potato beetle European corn borer Potato flea beetle Potato leafhopper Potato tuberworm Wireworms	2.0-3.0/acre (with 38-in. row spacing) or 0.143-0.218/1,000 linear feet of row (G)	Use restricted to New York state. Apply directly into the bottom of the seed furrow at planting.
Colorado potato beetle Potato flea beetle Potato leafhopper	0.5-1.0/acre (flow)	Northeast, North Central and Colorado only. Apply when insects appear. Do not make more than 8 applications/season. Do not apply more than 3 qt. to foliage if Furadan 10G were used at planting. Do not apply more than 1 qt./application. Do not apply within 10 days of harvest. Use ground equipment only.
Rice		1.0 ppm (rice and rice straw) (not more than 0.2 ppm carbamates). Do not apply more than once per season.
Dark field Mosquito (larvae)	0.45-0.6/acre (G)	Use restricted to Arkansas, Louisiana, Mississippi, and Texas. Apply from 1 day before to within 2 days after permanent flooding. For dark ricefield mosquito, application must be made within 2-4 days after flooding. Occasional tip burn may occur if propanil is also used. Do not make more than one application per season. Apply by air or ground equipment.
Rice water weevil	0.5/acre (G)	Use restricted to California. Preplant soil treatment. Apply to soil surface prior to flooding. Subsequent use of propanil may result in crop injury. Do not make more than one application per season. Apply by air or ground equipment.
	0.45-0.6/acre (G)	Use restricted to Arkansas, Louisiana, Mississippi, and Texas. Apply from 1 day before to within 21 days after permanent flooding. Occasional tip burn may occur if propanil is also used. Do not make more than one application per season. Apply by air or ground equipment.
Shorghum Greenbug	0.75-1.0/acre (G)	Use only on grain sorghum grown for forage. Apply in seed furrow or in a 7-inch band over the row.
Strawberry Root weevils	1.0-2.0/acre (flow)	Washington and Oregon, apply as 10 to 12 inch hand over the row after last harvest but before Oct. 1. Do not make more than one application per season.
Sugarcane		0.1 ppm. 17-Day preharvest interval through 0.75 lb/acre, broadcast application. Do not use in Hawaii. 4.0 lb/8,500 ft per season.

Table 27. (Continued)

Pest and site	Dosage (lb actual)	Tolerance, use, limitations
Sugarcane (continued)		
Nematodes (root-knot, stunt)	2.0-4.0/8, 500 linear feet of row (G)	Apply at planting time in a 15-in. band directly over planted cane just before covering with soil. For stubble cane apply in a 15-in. band over the stubble row within 1-2 weeks following harvest then cover with 1-2 in. of soil
Sugarcane borer	0.5-0.75/acre (WP, flow G)	Broadcast application. Check field weekly from early June through August. Make first application only after visible joints form and 5% or more of the plants are infested with young larvae feeding in or under the leaf sheath and which have not bored into stalks. Repeat whenever field checks indicate the infestation rate exceeds 5%.
Wireworms	2.0-4.0/acre (with 60-in. row spacing) or 0.2.-2.5/1,000 linear feet of row (G)	At planting soil application. Apply in a 15-in. band directly over planted cane and cover with soil. Do not use in Hawaii. Stubble treatment. Apply in a 15-in. band over the stubble row. Apply anytime after harvest until regrowth reaches 18 in. Cover with a 1-2 in. layer of soil. Covering with more than 2 in. of soil may reduce stand. For use in Florida only.
Sugar beet Root maggot	20/acre (G)	Apply in a 6- to 7-in. band and incorporate into top one in. of soil.
Tobacco (flue cured)		NF
Flea beetles Hornworms	6.0/acre (G)	Broadcast soil application before forming beds. Incorporate into top 4-6 in. of soil. Form beds and plant as usual. or
	4.0/acre (G)	Band application after forming beds. Apply in a 14-18 in. band over bed. Incorporate into top 4-6 in. of soil and reform bed. Plant as usual. This gives full season control of flea beetles and controls hornworms for approximately 60 days.
Nematodes (root-knot, stunt)	6.0/acre (G)	Before forming beds, apply granules broadcast over soil surface and incorporate 4-6 in. deep. Form beds and plant. or After forming beds, apply granules in a 14-18 in. band over the bed and incorporate to a depth of 4-6 in. Reform bed and plant. For flue-cured tobacco only.
Tobacco budworm Wireworms	6.0/acre (G)	Broadcast soil application before forming beds. Incorporate into top 4-6 in. of soil. Form beds and plant as usual. Claims are limited to aids in the control of the tobacco budworm.
Tobacco (Burley)		
Flea beetles	3.0-4.0/acre (G)	Broadcast granules over the soil surface prior to transplanting and incorporate with a suitable device.

Table 27. (Continued)

Site and pest	Dosage (lb actual)	Tolerance, use, limitations
Ornamentals		
(Woody shrubs, trees and vines)		
Cottonwood		
Cottonwood twig borer Cottonwood leaf beetle Clearwing borer	0.275-0.55/1,000 linear feet of row 12-in. row spacing - 1.0-2.0/acre (G)	For use in commercial plantings. Apply during June or July to the root zone of the cutting by the use of a subsoil applicator as a side-dress 10-12 in. from the trees in a continuous band on both sides of the trees.
	0.3/1,000 linear feet of row - 40 in. row spacing - 4.0/acre (G)	For use in nursery plantings. Apply in May or June to the root zone of the cutting by the use of a subsoil applicator as a sidedress 10-12 in. from the trees in a continuous band on both sides of the trees.
Siberian elm		
Elm leaf beetle	0.003 lb or 0.049 oz/in of girth at 3-4 ft height/tree (soluble packet)	Use limited to Arizona, Colorado, Kansas, Nebraska, New Mexico, Utah and Wyoming. Soil treatment. Measure circumference (girth) at 3-4 ft height and place holes in ground (using probing tool) evenly spaced around tree: If girth is: — Locate holes away from trunk: 1-10 in. — 1 ft 14-20 in. — 3 ft 24-40 in. — 6 and 12 ft (alternating) 44-80 in. — 10 and 12 ft (alternating) 80 in. and larger — 12 and 20 ft (alternating) Thoroughly soak area under trees. Determine proper location for holes and insert plugging tool in soil with a slight twisting motion. If soil is properly soaked, tool will enter soil easily. Push tool in soil to depth of black mark on stem of tool. Leave soil plug in stem as the next plug will force the preceding one out. Place soil plug by each hole. Drop one packet in each hole unopened. Place small amount of water on top of each packet. Replace soil plug immediately and compress with foot. Keep treated areas soaked with water for 14 days.
Forest, nonagricultural and wastelands		
Pine seedlings		
Pales weevil Pitch-eating weevil	0.05/half gallon water (flow)	Pretransplant root treatment. For use in pine plantations. Prepare and apply a 1% (w/w) actual slurry of clay to roots of pine seedlings. Treat roots by dipping or other suitable method which allows for a thorough coating. Keep roots moist until seedlings are transplanted. This amount treats 150-200 seedlings. Adequate ventilation is required for indoor treatment.
	1 teaspoon 10% (G)/seedling or 1.0 g/seedling (G)	Apply at transplanting. Distribute granules on soil in a 6-in. radius around each seedling. Cover granules with soil.

Table 28. Use of Carbofuran in the U.S. by Crops, 1971

Crop	Quantity used 1,000 Lb active ingredient	Quantity used Percent	Acreage treated 1,000 Acres	Acreage treated Percent
Corn	2,681	93.9	3,677	97.5
Rice[a]	164	5.7	78	2.1
Other field crops	4	0.2	7	0.2
Vegetables	2	0.1	8	0.2
Fruits and nuts	3	0.1	2	Negl.
Total	2,854	100.0	3,772	100.0

[a] The quantity of the compound may be upward biased or the rice acreage treated may be downward biased since the recommended application rate is only 0.5 lb/acre.

Source: U.S. Department of Agriculture (1974).

Table 29. Use of Carbofuran in the U.S. by Regions, 1971

Farm production region	Quantity used 1,000 Lb active ingredient	Percent	Acreage treated 1,000 Acres	Percent
Northeast[a]	59	2.1	79	2.1
Appalachian[b]	22	0.8	30	0.8
Southeast[c]	4	0.1	7	0.2
Delta States[d]	62	2.2	36	1.0
Corn Belt[e]	1,140	39.9	1,443	38.2
Lake States[f]	791	27.7	1,302	34.5
North Plains[g]	635	22.3	779	20.7
South Plains[h]	-	-	-	-
Mountain[i]	38	1.3	54	1.4
Pacific[j]	103	3.6	42	1.1
Total	2,854	100.0	3,772	100.0

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a/ Maine, New Hampshire, Massachusetts, Vermont, Connecticut, Rhode Island, New York, Delaware, Pennsylvania, Maryland, New Jersey.

b/ Kentucky, Tennessee, West Virginia, Virginia, North Carolina.

c/ Alabama, Georgia, South Carolina, Florida.

d/ Arkansas, Louisiana, Mississippi.

e/ Iowa, Missouri, Illinois, Indiana, Ohio.

f/ Minnesota, Wisconsin, Michigan.

g/ North Dakota, South Dakota, Nebraska, Kansas.

h/ Texas, Oklahoma.

i/ Montana, Idaho, Wyoming, Nevada, Utah, Colorado, Arizona, New Mexico.

j/ Washington, Oregon, California.

Source: U.S. Department of Agriculture (1974). (Application rates per acre added by RvR Consultants.)

Table 30. Use of Carbofuran in California by Major Crops and Other Uses, 1970-1974

Year / Crop/use	1970	1971	1972	1973	1974
	1,000 lb of active ingredient				
Alfalfa[a]	-	0.1	2.7	94.0	135.7
Rice	8.8	8.7	7.8	11.3	10.4
Cotton[b]	-	0.4	-	1.1	-
All other crops and uses	0.7	0.3	0.1	0.2	-
Total	9.5	9.5	10.6	106.6	146.1

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[a] Including alfalfa for hay and for seed.
[b] Carbofuran is not registered for use on cotton.

Source: California Department of Agriculture (1973, 1974 and 1975).

Table 31. Use of Carbofuran in California in 1972, 1973 and 1974 by Crops and Other Uses, Applications, Quantities, and Acres Treated

Commodity	Applications	Pound active ingredient	Acres
1972			
Alfalfa	187	2,719.29	18,687.50
Alfalfa for seed	1	21.02	24.00
Rice	343	7,849.20	15,748.90
Tomato	1	1.87	50.00
University of California	—	0.11	—
Total	532	10,591.49	34,510.40
1973			
Alfalfa	2,744	93,720.02	268,279.50
Alfalfa for seed	5	229.50	304.00
Almond	2	16.19	37.00
Apple	1	17.87	51.00
Apricot	1	15.32	35.00
Beans, dry edible	5	51.66	76.00
Cotton	1	1,114.27	53.00
Fallow (open ground)	1	45.00	90.00
Nonagricultural areas	1	0.03	12.00
Peach	1	1.75	8.00
Potato	8	31.52	36.00
Rice	224	11,309.73	18,150.70
Soil (fumigation only)	1	5.00	10.00
University of California		0.28	
Water areas	2	15.76	18.00
Total	2,997	106,573.90	287,160.20
1974			
Alfalfa	2,841	135,670.12	267,605.63
Rice	241	10,437.11	21,075.30
Rice	1	0.20	40.00
Total	3,082	146,107.43	288,680.93

Source: California Department of Agriculture (1971 to 1975).

Table 32. Estimated Uses of Carbofuran in the U.S.
by Regions in 1971, 1972 and 1974

Year Region	1971	1972	1974
	1,000 Lb of active ingredient		
Northeast[a]	60	100	125
Southeast[b]	30	100	125
North central[c]	2,570	4,400	6,300
South central[d]	60	200	250
West[e]	140	200	400
Total	2,860	5,000	7,200

a/ New England States, New York, New Jersey, Pennsylvania.

b/ Maryland, Delaware, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida.

c/ Ohio, Indiana, Illinois, Minnesota, Wisconsin, Michigan, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas.

d/ Kentucky, Tennessee, Arkansas, Louisiana, Mississippi, Alabama, Oklahoma, Texas.

e/ Montana, Idaho, Wyoming, Colorado, Utah, Washington, Oregon, Alaska, New Mexico, Nevada, Arizona, California, Hawaii.

Sources: 1971 - U.S. Department of Agriculture (1974).
1972 - von Rumker et al. (1974).
1974 - RvR estimates; see text.

Note: The estimates for 1971 and those for 1972 and 1974 originate from different sources and were obtained by different methods and are therefore not directly comparable; see text.

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PART III. MINIECONOMIC REVIEW

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This section contains a general assessment of the efficacy and cost effectiveness of carbofuran. Data on the production of carbofuran in the United States, as well as an analysis of its use patterns at the regional level, were developed as part of the Scientific Review (Part II) of this report. The section summarizes rather than interprets data reviewed.

Introduction

The efficacy and cost effectiveness of a specific pesticide applied to cropland should be measurable in terms of the value of increased yield or improved quality or in terms of reduced costs associated with the pesticide's use. Therefore, one should be able to select a test plot of a given crop, treat it with a pesticide, and compare its yield with a similar untreated plot. The difference in yield should be the increase related to the use of the pesticide. The increased income (i.e., the yield increase multiplied by the selling price of the commodity) less the additional cost (i.e., the pesticide, its application, and the harvesting of the increased yield) is the net economic benefit related to the use of the pesticide.

Unfortunately, this method has many limitations. The data derived is incomplete and should be looked on with caution. Review of the literature and EPA registration files revealed pesticide-treated versus nontreated crop experiments are conducted by many of the state agricultural experimental stations. Only a few tests, however, have attempted to measure increased yield and most of the yield information is found with a few crops such as cotton, corn, potatoes, sorghum, and selected vegetables. Most crop experiments measure the reduction in pest populations which cannot be directly related to yield.

Even yield data from the test plots is only marginally reliable, since these tests are conducted under field conditions that may never be duplicated again or may not be representative of actual field practices. Each experiment is somewhat unique since yield is affected by rainfall, fertilizer use, severe weather conditions, soil type, region of the country, pest infestation levels, and the rate, frequency and method of pesticide application.

Because of the above factors, yield tests at different locations and in different years will show wide variations ranging from declines to significant increases. For example, in a year of heavy pest infestation, pesticide use can result in a high yield increase because of extensive damage in the untreated test plot. Conversely, in a year of light infestation, the yield increase will be slight.

The use of market price to estimate the value received by the producer also has limitations. If the use of a pesticide causes an increase in the national production, then the market price should decline. According to Headley and Lewis (1967), a 1% increase in quantity marketed has at times resulted in a greater than 1% decrease in price. Thus, the marginal revenue from the increased yield would be a better measure of the value received.

A third limitation to the quantification of the economic costs and benefits is the limited data on the pesticide quantities used by crop or pest, the number of acres treated, and the number of applications. In most cases the amount of carbofuran used on different crops is not available.

As a result of these limitations, an overall economic benefit for a crop-pest combination cannot be determined. Where applicable, a range of the potential economic benefits derived from the use of the pesticide for control of a specific pest on a crop is developed. This economic benefit or loss is measured in dollars per acre for the highest and lowest yield found in reviewed experimental tests. The highest and lowest yield increases are multiplied by the price of the crop and reduced by the cost of the pesticide and its application to give a range of net economic benefits.

Carbofuran is a broad spectrum insecticide and nematicide available as a flowable or granular formulation. The chemical may be applied at planting time or as a foliar treatment (post-planting) depending on the crop and target pest. It is registered for use on alfalfa, corn, peanuts, peppers, potatoes, rice, sugarcane, and tobacco. Target pests of carbofuran include armyworms, corn borers, nematodes, rootworms, wireworms, weevils, aphids, lygus bugs, beetles, leafhoppers, tuberworms, grasshoppers, horn worms, and tobacco budworms. The degree of control varies with the method, rate and timing of application, the specific pest, and the crop. The use of carbofuran has been shown to give excellent control of several pests and to increase yields significantly.

Carbofuran prices are estimated at $4.55/lb AI for granular formulations and $6.86/lb AI for 4F formulations (Shmerler, 1975).

For the purpose of this analysis, carbofuran application costs are neglected when carbofuran is applied with the seed at the time of planting; the incremental costs would be insignificant. Cost for incorporation into the soil is estimated to be $2.50/acre and the estimated cost for foliar application is $1.50/acre. All application rates are reported in pounds of active ingredient.

Efficacy of Pest Control on Alfalfa

Carbofuran is recommended for control of the alfalfa snout beetle, alfalfa weevil, Egyptian alfalfa weevil larvae, lygus bugs, and the pea aphid.

Depew (1969) evaluated several insecticides for control of the weevil in tests at Garden City, Kansas, during 1967 and 1968. Carbofuran EC at 0.25 lb/acre provided 98% control after 14 days. In a second test, carbofuran EC at 0.5 lb/acre gave 100% control after 7 days and 94% control after 28 days.

Summers et al. (1971) found in alfalfa weevil tests at Ithaca, New York, that carbofuran at 1.0 lb/acre sprayed on alfalfa was superior to other insecticides used in the test and that effects of the insecticide were evident 4 weeks after application. The carbofuran-treated plots looked excellent and rated 1 on a scale of 1 (no visible damage) to 10 (crop destroyed). Carbofuran also gave 95% control of aphids. Similar results were achieved in a second experiment conducted later in the season.

The Egyptian alfalfa weevil is a serious pest of alfalfa in California. Losses from this weevil in 1970 exceeded $6 million (Summers and Cothran, 1972). Several insecticides for control of the weevil at Strathmore, California, were evaluated during 1971. Carbofuran sprayed on a plot at a rate of 1 lb/acre as early as 80 days prior to cutting gave effective control. The mean damage rating on a scale of 1 (no damage) to 10 (crop destroyed) was 2.0 for carbofuran and 7.3 for the untreated plot.

Johansen and Eves (1972) evaluated the effect of aerial applications at 1.0 lb/acre of prebloom sprays on lygus bugs and aphids in alfalfa fields at Zillah, Washington. Carbofuran was quite effective against lygus bugs which increased to only 4.4 nymphs per sweep at the end of 33 days. However, aphid counts gradually increased (to 232.0/sweep) after 33 days. At this population level, the field needed retreatment for both pests.

Cost Effectiveness of Pest Control

The yield effects related to the use of carbofuran on alfalfa ranged from a decline of .08 to an increase of 1.18 tons/acre. At a 1971 to 1973 average hay price of $33.33/ton (U.S. Department of Agriculture, 1974), the net economic benefits associated with the use of carbofuran on alfalfa ranged from a loss of $11.03 to a gain of $34.97/acre. These results are summarized in Table 33.

Efficacy of Pest Control on Field Corn

Carbofuran formulations are registered for control of several pests that attack field corn. These include the armyworm and fall armyworm; European and southwestern corn borers; flea beetles; the dagger, lance, lesion, root-knot, spiral, sting, stunt and stubby root-knot nematodes; corn rootworms (northern, southern, and western) and wireworms.

The western corn rootworm is a serious pest in the midwestern corn belt. Hills and Peters (1972) evaluated several insecticides and application methods at Newell, Iowa, in 1969. Carbofuran was applied at a rate of 1.0 lb/acre in liquid and granular formulations to De Kalb XL306 seed corn. With an assumed acceptable adjusted root damage rating equal to or less than 2.5, carbofuran performed favorably with damage ratings ranging from 1.62 to 2.23.

Musick and Fairchild (1968) concluded that carbofuran, at rates varying from 0.25 to 1.0 lb/acre, would be recommended for control of the western corn rootworm larvae in Missouri. Carbofuran was applied with the seed at planting and was rated for control of root damage. All tests were significantly better than an untreated check at the 5% probability level.

Apple et al. (1969) found that 0.84 kg/ha (0.77 lb/acre) of carbofuran provided outstanding protection from the northern corn rootworm in tests during 1968. The average number of larvae were reduced 99.6% compared to an untreated check.

Petty and Kuhlman (1972) reported on corn rootworm control tests in Illinois from 1968 to 1971. For the 1971 tests, carbofuran 10% granules banded at 0.8 lb/acre gave the highest control (77.7%) of all materials evaluated and resulted an 11.4% yield enhancement. The summary of tests over the 4-yr period showed that carbofuran averaged 84.6% control and resulted in a yield enhancement of 12.3%. Kuhlman and Petty (1973) reported on 1972 tests in Illinois which demonstrated that carbofuran 10G banded at 1.0 lb/acre gave an average of 92% larvae control and increased yields by 5.8%.

The southwestern corn borer is a major pest in certain states. In pest control tests, Henderson and Davis (1970) studied 4 insecticides at State College and Holly Springs, Mississippi, from 1966 to 1968. The results showed that 4 applications of 3% carbofuran granules applied to the foliage at 0.5 lb/acre reduced borer infestation by 48 to 84% and stalk girdling by 70 to 95%. Yield changes compared to untreated plots ranged from a loss of 2.0 bu/acre to a gain of 18.0 bu/acre. In 1968 tests with 4 applications of 1.0 and 0.5 lb/acre/application reduced borer infestation from 58 to 95%. Yield changes ranged from a 1.0 bu/acre reduction to a 10.0 bu/acre increase over the untreated plot. Some of the use rates in this test were above the quantities registered for use.

Keaster (1972) found that carbofuran 10G applied at rates of 1.44 to 2.0 lb/acre to the foliage of corn at Portageville, Missouri, in 1968 reduced the amount of borer girdling by 49 tc 90%. Yield effects varied from a loss of 6.6 bu/acre to a gain of 21.8 bu/acre.

The European corn borer has been effectively controlled with carbofuran. Harding et al. (1968) found that 0.25 lb/acre provided 91% control of the first-generation borer and 78% control of the second-generation borer in field tests in 1966. Berry et al. (1972) conducted similar tests and reported 75 to 81% control of first-generation borers with a 3% granular formulation at rates of 0.25, 0.50, and 1.0 lb/acre. Control of second-generation borers was not as good, ranging from 21% with an application of 0.25 lb/acre granules to 78% with 1.0 lb/acre of 3% granules.

Wedderburn et al. (1973) observed that carbofuran granules applied at 0.75 lb/acre to the whorls reduced first-generation corn borers by 77% in tests at Mead, Nebraska, in 1971. In a second test, carbofuran 10% granules at 2.0 lb/acre applied either to the furrow or band reduced the number of tunnels by 42 to 71%.

Kuhlman and Petty (1972) found that carbofuran at 1.0 lb/acre applied at planting with corn in Illinois did not control the first-generation borer. However, 90% control was achieved at rates of 2.0 lb/acre and 100% control occurred at 3.0 lb/acre.

Musick and Suttle (1973) evaluated carbofuran for control of the armyworm. Carbofuran 10G was applied at rates of 1.2, 2.4, and 4.8 oz AI/1,000 linear feet of row at planting. They found that the effectiveness varied with the date of treatment and rate of application. An application rate of 2.4 oz/1,000 linear feet of row was required at planting for maximum suppression of the armyworm.

Kuhlman (1974) found that carbofuran applied with no-till corn at 1.0 lb/acre achieved 100% control. These tests were conducted in Illinois in 1973 when armyworm infestation was light.

Kuhlman and Petty (1972) found that wireworm control was poor with carbofuran. Tests in Illinois in 1971 at 1.0 lb/acre applied with corn at planting showed an average control of 13.3%. These results were confirmed by Sechriest and Sherrod (1973) who found that 1.3 lb/acre of carbofuran banded on corn for wireworm control was not significantly different at the 5% level from an untreated plot. The application rates were lower than the 2.0 to 4.0 lb/acre recommended rate.

Nematode control was evaluated by Dickson and Johnson (1972). Although control of sting and lesion nematodes with 10G carbofuran at a rate from 1.0 to 2.0 lb/acre was slightly better than the untreated plots it was not significantly different at the 5% probability level. Yield, however, increased from 13 to 22 bu/acre. Arnett (1973) found similar results with carbofuran 10G at the 2 lb/acre rate. Yields increased from 26.5 to 27.2 bu/acre, but stubby rootknot and spiral nematodes were not controlled.

Cost Effectiveness of Pest Control

The range of yield changes due to the use of carbofuran varied from a loss of 6.6 to a gain of 49.4 bu/acre as a result of several tests on corn. With a 1971 to 1973 average corn price of $2.01/bu (U.S. Department of Agriculture, 1974), the net economic benefits associated with the use of carbofuran on corn after subtracting pesticide and application costs ranged from a loss of $22.44/acre to a gain of $48.09/acre. Reduction in yields only occurred in 2 of the tests. These results are summarized in Table 34.

Efficacy of Pest Control on Peanuts

Carbofuran is registered for control of thrips, nematodes (lesion, ring, root-knot, sting, and stunt), the potato leafhopper, and the southern corn rootworm on peanuts. Several references on the efficacy and yield changes associated with carbofuran applications on peanuts were available from tests conducted by the agricultural experiment stations at Tifton, Georgia; Virginia Polytechnic Institute at Blacksburg and Holland, Virginia; and Oklahoma State University at Stillwater, Oklahoma. Data was available on all of the above pests with the exception of the potato leafhopper. Most tests measured carbofuran efficacy against several pests so that yield changes could not be identified with control of any single pest.

Osborne (1970) conducted several tests at various locations in Virginia comparing carbofuran to other pesticides for control of root-knot, sting, stunt, and ring nematodes as well as control of thrips on peanuts. Application rates varied from 2 to 5 lb/acre. They were applied in an 18 in wide band and incorporated 6 to 8 in deep. Control of sting nematodes at the 2.0 lb/acre rate ranged from 72 to 92%, and only slight damage from thrips was noticed. Thrips damage was rated 15 on a scale of 10 (no damage) to 30 (severe damage). Yield increases ranged from 300 to 1,028 lb/acre.

Smith (1972) conducted tests at Courtland, Virginia, and Cyprus Chapel, Virginia, in 1971 comparing insecticides for control of thrips and ring nematodes on peanuts. Carbofuran was applied in 14-in bands at a depth of 8 in. At Courtland, carbofuran 10G was applied at planting at 1.0 and 4.0 lb/acre. Although thrips control increased 63% at both rates, ring nematodes were not controlled at the 1.0 lb/acre rate. Yields were also lower by 357 and 412 lb/acre. Results were similar at Cyprus Chapel, although yield effects were not reported.

Smith (1971) also evaluated several insecticides for the control of southern corn rootworm on peanuts grown in Virginia from 1965 to 1967. Carbofuran applied at planting at rates from 1.0 to 4.0 lb/acre (the latter rate being higher than the current recommended rate). The 1.0 lb rate provided control ranging from 1.8 to 9.3% damaged fruit. The damage to the comparable test plots was 7.1 and 29.8%, respectively. Yield increase at 1.0 lb/acre was 7.0%.

Several tests were conducted in Georgia to evaluate the ability of carbofuran to control ring, root lesion, and root-knot nematodes, thrips, and leafhoppers. Minton et al. (1969) found that the number of ring nematodes in a peanut plot treated with 3.0 lb/acre of carbofuran had more nematodes than an untreated test plot. Minton and Morgan (1970) reported more effective control of ring nematodes with carbofuran 10G applied at planting of 5.0 lb/acre than at 3.0 lb/acre. Control increased 34% at the 5.0 lb rate. (A 4.0 lb/acre rate is currently recommended.)

Carbofuran effectively controlled the lesion nematodes as measured by a pod lesion index. On a scale of 1 to 3 (3 = severely discolored), carbofuran-treated peanuts were significantly better than the untreated check at the 5% level of significance. The rating index ranged from 1.0 to 1.8 at rates of 3.0 to 5.0 lb/acre. Yields increased from 114 to 232 lb/acre (Minton et al., 1970).

Morgan and Minton (1970) concluded that high yields of peanuts were directly related to control of root-knot nematodes. This was supported by Minton and Morgan (1971). Carbofuran applied at a rate of 5.0 lb/acre (which is higher than registered use rates) in this test resulted in a peanut yield of 2,806 lb/acre compared to a rototilled check plot yield of 1,469 lb/acre. Galling of roots was measured by an index of 1 to 5 with 1 representing the least galled and the 5 the most severely galled. The index for the carbofuran plot was 2.9, compared to 4.7 for the check.

Carbofuran controlled thrips in most tests, but little relation was found between thrips control and yields (Minton et al., 1969).

Sturgeon and Shackelford (1972) reported that carbofuran at 2.0 and 4.0 lb/acre applied with the seed effectively reduced nematode populations and increased yields from 423 to 485 lb/acre over an untreated plot.

Cost Effectiveness of Pest Control

The range of yield changes associated with the use of carbofuran varied from a loss of 412 lb/acre to a gain of 1,137 lb/acre. At an average 1971 to 1973 price of 14.7¢/lb for peanuts (U.S. Department of Agriculture, 1974), economic benefits after subtracting pesticide and application costs ranged from a loss of $70.68/acre to a gain of $171.29/acre. Most of the test results showed positive yield increases. These results are summarized in Table 35.

Efficacy of Pest Control on Peppers

Carbofuran is recommended for control of the European corn borer and green peach aphid on peppers. Since 1951 these pests have caused serious economic damage to sweet peppers in Delaware and neighboring states.

Ryder et al. (1969) evaluated insecticides for control of the borer and aphids at Bridgeville, Delaware, in 1968. They found that either single or double applications of carbofuran 10G side-dressed at 3 lb/acre reduced green peach aphids by 74% for 8 weeks. Control of borers ranged from 70 to 90% at the 3.0 lb rate. Yields increased by 2.9 tons/acre over the untreated plot.

Burbutis et al. (1972) tested carbofuran for control of the green peach aphid in several tests in Delaware between 1969 to 1971. Single and double applications of carbofuran granules side-dressed in a band at rates varying from 1 to 4 lb/acre reduced aphid populations by 56 to 95%. Burbutis and Lesiewicz (1974), in 1971 tests at Bridgeville, Delaware, found that 2 lb/acre of carbofuran 10G, followed by a 3 lb/acre application, reduced European corn borer infestation later to 1% (compared to 30% for the check) and increased yields by 3.6 tons/acre. Hale and Shorey (1971) conducted tests at Santa Maria, California, from 1965 to 1969. They found that carbofuran foliar sprays at 0.5 and 1.0 lb/acre reduced aphids by 87 to 100% 14 days after treatment and up to 99% 28 days after treatment.

Cost Effectiveness of Pest Control

Pepper yield changes, due to the use of carbofuran, varied from a gain of 22 cwt to 82 cwt/acre when compared to untreated test plots. At a 1971 to 1973 average price of $12.97/cwt for peppers (U.S. Department of Agriculture, 1974) and a cost of $4.55/lb AI for carbofuran, and an application cost of $12.50/acre, the net economic benefits ranged from a gain of $269.19 to $1,035.79/acre.

Efficacy of Pest Control on Potatoes

Carbofuran is registered for control of aphids, the Colorado potato beetle, European corn borer, potato flea beetle, potato leafhoppers, potato tuberworm and wireworms on potatoes.

Onsager (1969) tested several insecticides at Quincy, Washington, in 1966 and George, Washington, in 1967. Carbofuran at rates of 2.2 lb/acre provided wireworm control and reduced the degree of injury to tubers by 71%. However, there were no significant differences in yields. Onsager and Foiles (1970) found that carbofuran applied by band application at 2.3 lb/acre was 27 to 64% more effective against wireworms than broadcast application at 4.0 to 8.0 lb/acre. (These latter rates are greater than registered uses.) No significant difference in yields was observed.

Day (1970) found that 5.0 lb/acre (3.0 lb/acre is the recommended rate) carbofuran granules broadcast on the soil gave 94% initial control of the southern potato wireworm. Control, however, declined to 45% by the end of 53 days. Day and Crosby (1972) found that carbofuran at 2.0 lb/acre produced erratic results in several experiments between 1965 and 1969 in South Carolina. Control varied from 24 to 100%.

Hofmaster and Waterfield (1972) evaluated insecticides for control of the Colorado potato beetle in several tests in Virginia. At Painter, Virginia, in 1967, 2.0 lb/acre of carbofuran were banded on each side of the row and effectively controlled the beetle for 120 days. Only 11 larvae/10 hills remained, whereas the plants that were not treated were defoliated. Tests during 1968 to 1971 showed similar reductions in larvae. In 1970, heavy infestations of the beetle destroyed the check plot resulting in significantly increased yields in the treated plots.

Chapman (1971) tested 2 formulations of carbofuran (4F and 10G) at 3 different rates of application (.5 lb/acre, 1.0 lb/acre and 3.0 lb/acre) to control flea beetles. Yield increases ranged from 25 cwt/acre for 3.0 lb/acre of a 10G formulation applied in-furrow to 78 cwt/acre for .5 lb/acre of a 4F formulation that was applied as a spray. Carbofuran 10G applied at 3.0 lb/acre gave complete control of the flea beetles and provided commercial control of aphids for 71 days after treatment.

FMC (1971) tested a 10G formulation of carbofuran for control of the green peach aphid and the Colorado potato beetle. A banded application of 1.18 lb/acre enhanced the potato yield by 72 cwt/acre when the green peach aphid was the target pest. With an application rate of 3.0 lb/acre directed at the Colorado potato beetle, the yield per acre was increased by 85 cwt.

Cost Effectiveness of Pest Control

The range of potato yield increases related to the use of carbofuran varied from 25 to 213 cwt/acre when compared to untreated potato test plots. At a 1971 to 1973 average price of $2.99/cwt for potatoes (Agricultural Statistics, 1974), net economic benefits after subtracting pesticide and application costs ranged from $61.10 to $625.27/acre. Results are summarized in Table 36.

Efficacy of Pest Control on Rice

Carbofuran is recommended for control of the rice water weevil and mosquito larvae.

Donoso-Lopez and Grigarick (1969) demonstrated that preplant treatment of rice fields with carbofuran at 1.0 lb/acre AI effectively controlled adult weevils (78% mortality) on rice seedlings up to 4 weeks following the applications. After 6 weeks mortality still occurred, but was reduced to 43%. At rates of 0.25 and 0.50 lb AI, mortality was less but not significantly so.

Gifford et al. (1975) evaluated carbofuran in several Louisiana parishes between 1970 and 1972. They concluded that a single broadcast application of 3% carbofuran granules at a rate of 0.5 lb/acre AI applied as much as 5 weeks after the rice seedlings are flooded will reduce infestations of the rice water weevil larvae established in the root systems. Yield increases per acre of rough rice ranged from 86 to 614 lb.

The dark rice field mosquito breeds exclusively in the rice-producing areas of Louisiana. Craven and Steelman (1968) evaluated several insecticides for control of the mosquito at Crowley, Louisiana, in 1967. Propanil at 3.0 lb/acre was also applied with all treatments. The mixture with carbofuran EC at 0.1 lb/acre applied 26 days after planting was phytotoxic to the plants; the control was only 26.4% which was less than in the check plot. Carbofuran at 0.05 lb/acre gave 47.0% control and phytotoxicity was not evident.

Lancaster and Tugwell (1969) found that carbofuran 10% granules applied to the soil prior to the first watering of rice fields completely eliminated the larvae of the southern house mosquito in tests at Stuttgart, Arkansas, in 1967. Similar results were also obtained in 1968 tests.

Cost Effectiveness of Pest Control

Several tests were conducted to determine yield effects of carbofuran for rice water weevil control. The results of these tests showed that yield effects ranged from a loss of 199 lb/acre to a gain of 1,614 lb/acre.

With a 1971 to 1973 average price of $8.72/cwt for rice (U.S. Department of Agriculture, 1974), economic benefits after subtracting pesticide and application costs ranged from a loss of $20.88/acre to a gain of $50.01/acre. Most of the tests showed positive yield changes. These results are summarized in Table 37.

Efficacy of Pest Control on Sugarcane

Carbofuran is recommended for control of the sugarcane borer, wireworms, and root-knot and stunt nematodes on sugarcane. Only one study was found which evaluated insecticides for control of the sugarcane borer. Fuchs et al. (1973) found that carbofuran at 0.75 lb/acre applied as an aerial spray was significantly more effective at the 5% level of probability than no treatment. Control of the borer, as measured by the percent of bored internodes, was 52% better than the untreated check.

Tests at the Everglades Experimental Station in Belle Glade, Florida, in 1966 showed that carbofuran for nematode control gave a 36.5% yield increase at an 8.0 lb/acre rate and 37.8% yield increase at a 16.0 lb/acre rate (Applewhite, 1969a).

Tests at Canal Point, Florida, from 1966 to 1967 showed that a 3.8 lb/-acre carbofuran in a banded application at planting gave better than 90% control of wireworms, and it increased yields by 34.1 tons/acre (Applewhite, 1969b).

In a 1971 Belle Glade, Florida, experiment (Metz, 1973a), 2 granular formulations (5G and 10G) of carbofuran were applied at rates of 2.0 and 4.0 lb/acre to control wireworms in stubble crop sugarcane grown in a muck soil. The 4 lb/acre rate was more efficacious than the 2 lb/acre rate, with wireworm control ranging from 52.2% to 82.6% 40 days after treatment. Increases in millable stalks/acre for all formulations ranged from 38.5% to 51.9%.

In a 1971/1972 Lantana, Florida, test (Metz, 1973a), 1 flowable and 2 granular formulations (4F, 10G, and 5G) of carbofuran were applied in-furrow at rates of 2.0 and 4.0 lb/acre to control wireworms in sugarcane. All formulations and application rates completely controlled the wireworms, but the largest yields resulted from the 4F formulations. Applied at 2 and 4 lb/acre, the 4F formulations increased the millable stalks/acre by 109.6% and 105.9%, respectively.

Cost Effectiveness of Pest Control

Yield increases related to the use of carbofuran on sugarcane ranged from 2.9 to 15.0 tons/acre. At a 1971 to 1973 average sugarcane price of $12.53/ton (U.S. Department of Agriculture, 1974), a carbofuran cost of $4.55/lb AI and an application cost of $2.50/acre, net economic benefits ranged from $38.37 to $172.48/acre. These results are summarized in Table 38.

Efficacy of Pest Control on Tobacco

Mistric and Smith (1972) found that foliar damage to newly set flue-cured tobacco plants by overwintered flea beetles was reduced by 97% with 4.1 lb/acre of carbofuran. Mistric and Smith (1973) also achieved 76% flea beetle control up to 16 weeks with 4.2 lb/acre of carbofuran applied prior to transplanting. The authors concluded that carbofuran was effective against all major insects attacking flue-cured tobacco. These insects include the tobacco wireworm, southern potato wireworm, tobacco flea beetle, tobacco budworm, and tobacco hornworm.

Dominick (1968) compared several insecticides for the control of the hornworm on tobacco. Carbofuran applied as a foliar spray at 1.0 lb/acre produced tobacco that remained free from hornworms during the 21-day test period. Mistric and Smith (1973) found in tests in Clayton, North Carolina, during 1965-1967 that a pretransplant treatment of 4.2 lb/acre (4.0 lb rate as recommended) carbofuran gave 96% control 31 days after transplanting, but its effectiveness decreased rapidly by the eleventh week.

Girardeau (1971) evaluated carbofuran for control of the tobacco budworm in experiments at Tifton, Georgia, in 1968 and 1969. The results of these tests showed that plots treated with carbofuran at 6 lb/acre had the lowest number of damaged plants on each observation date throughout the season. Treatments at 3.0 lb or less per acre apparently became ineffective after the seventh and eighth week after application. They concluded that rates of 4 to 6 lb/acre of carbofuran 10G would provide good season-long protection as measured by percent of leaves lost to the budworm. This loss ranged from 2.6 to 4.2%. Mistric and Smith (1973) applied carbofuran prior to transplanting at rates of 4.0 to 4.5 lb/acre and obtained 38 to 52% budworm control for 5 weeks in 2 out of 3 tests when the carbofuran was applied prior to transplanting. Carbofuran control of the budworm in one of the 2 post-transplant experiments was 70%.

Cost Effectiveness of Pest Control

The yield increases related to the use of carbofuran on tobacco ranged from 102 to 578 dried lb/acre. At a 1971 to 1973 average tobacco price of $.839/lb (U.S. Department of Agriculture, 1974), a carbofuran cost of $4.55/-lb AI, and an application cost of $2.50/acre, net economic benefits ranged from $55.78 to $455.14/acre. These results are summarized in Table 39.

Table 33. Summary of Carbofuran Tests on Alfalfa.

Pest	Applications				Yield Increase (dried tons/acre)b/	Additional Income at $33.33/ton ($/acre)	Carbofuran Costsc/ ($/acre)	Application Costd/ ($/acre)	Economic Benefit ($/acre)	Source
	Formulation	Methoda/	Rate (lb/acre)	No.						
Alfalfa weevil	4F	A	.5	1	.6	20.00	3.43	1.00	15.57	Brent and Broadus, 1973
Alfalfa weevil.	4F	A	.5	1	.11	3.71	3.43	1.00	(.72)e/	Broadus, 1973b
Alfalfa weevil	4F	FS	.5	1	.15	5.00	3.43	1.50	.07	Broadus, 1973a
Alfalfa weevil	4F	FS	.5	1	-	-	3.43	1.50	(4.93)e/	Hasuda and Broadus, 1973
Alfalfa weevil	4F	A	1.0	1	.79	26.39	6.86	1.00	18.53	Broadus, 1973b
Alfalfa weevil	4F	FS	1.0	1	1.3	43.33	6.86	1.50	34.97	Pienkowski, 1974
Alfalfa weevil	4F	FS	1.0	1	1.18	39.33	6.86	1.50	30.97	Pienkowski, 1974
Alfalfa weevil	4F	FS	1.0	1	.3	10.00	6.86	1.50	1.64	Broadus, 1973a
Alfalfa weevil	4F	FS	1.0	1	-	-	6.86	1.50	(8.36)e/	Hasuda and Broadus, 1973
Alfalfa weevil	4F	FS	1.0	1	(.08)	(2.67)	6.86	1.50	(11.03)e/	Pienkowski, 1974

a/ A = Aerially applied.
FS = Foliar spray.

b/ Yield is expressed as a dried weight, which is approximately 25% of the wet weight.

c/ 4F formulation - $6.86/lb (Shmerler, 1975).

d/ Aerial application - $1.00/acre; Spray application - $1.50/acre.

e/ Data in parentheses indicates decreases in yield, income, and economic benefit.

Table 34. Summary of Carbofuran Tests on Corn.

Test	Applications				Yield Increase[b] (bu/acre)	Additional Income[b] at $1.67/bu ($/acre)	Carbofuran Cost[c] ($/acre)	Application Cost[d] ($/acre)	Economic Benefit[b] ($/acre)	Source
	Formulation	Method[a]	Rate (lb/acre)	No.						
Nematodes	10G	B	1.0	1	[illegible]	21.71	4.55	2.50	14.66	Dickson and Johnson (1972)
Nematodes	10G	B	2.0	1	22	36.74	9.10	2.50	25.14	Dickson and Johnson (1972)
Nematodes	10G	B	1.0	1	22	36.[illegible]	4.55	-	32.19	Dickson and Johnson (1972)
Nematodes	10G	B	1.0	1	14	23.38	4.55	-	18.83	Dickson and Johnson (1972)
Nematodes	10G	B	2.0	1	27.2	45.24	9.10	2.50	33.64	Arnett (1973)
Nematodes	10G	B	2.0	1	26.5	44.26	9.10	2.50	32.66	Arnett (1973)
Nematodes	4F	B	2.0	1	37	61.79	13.72	-	48.07	Dickson and Johnson (1973)
Nematodes	10G	B	2.0	1	32	53.44	9.10	-	44.34	Dickson and Johnson (1973)
Nematodes	10G	B	1.0	1	21	35.07	4.55	-	30.52	Dickson and Johnson (1973)
Nematodes	10G	B	2.0	1	10	16.70	9.10	-	7.60	Dickson and Johnson (1973)
Nematodes	10G	B	2.0	1	32	53.44	9.10	-	44.34	Johnson et al. (1973)
Nematodes	10G	B	2.0	1	20	33.40	9.10	2.50	21.80	Johnson et al. (1973)
Nematodes	10G	B	2.0	1	21	35.07	9.10	-	25.97	Dickson et al. (1973)
Southwestern corn borer	10G	F	3.0	1	21.9	36.57	13.65	-	22.92	Keaster and Fairchild (1968)
Southwestern corn borer	10G	F	2.0	1	25.2	42.08	9.10	-	32.98	Keaster and Fairchild (1968)
Southwestern corn borer	10G	F	3.0	1	15.5	25.88	13.65	-	12.23	Keaster and Fairchild (1968)
Southwestern corn borer	10G	F	2.0	1	23.0	38.41	9.10	-	29.31	Keaster and Fairchild (1968)
Southwestern corn borer	10G	F	3.0	1	18.2	30.39	13.65	-	16.74	Keaster and Fairchild (1968)
Southwestern corn borer	10G	F	2.0	1	19.9	33.23	9.10	-	24.13	Keaster and Fairchild (1968)
Southwestern corn borer	10G	F	3.0	1	36.6	61.12	13.65	-	47.47	Keaster and Fairchild (1968)
Southwestern corn borer	10G	F	2.0	1	49.4	82.50	9.10	-	73.40	Keaster and Fairchild (1968)
Southwestern corn borer	10G	FG	1	2	21.8	36.41	13.65	5.00	17.76	Keaster (1972)
Southwestern corn borer	10G	FG	1	2	14.7	24.55	9.10	5.00	10.45	Keaster (1972)
Southwestern corn borer	10G	FG	0.72	2	(6.6)	(11.02)	6.55	5.00	(22.57)	Keaster (1972)
Southwestern corn borer	10G	FG	0.72	2	6.9	11.52	6.55	5.00	(.03)	Keaster (1972)
Southwestern corn borer	3G	FG	0.5	4	9.0	15.03	9.10	10.00	(4.07)	Henderson and Davis (1970)
Southwestern corn borer	3G	FG	0.5	4	15.0	25.05	9.10	10.00	5.95	Henderson and Davis (1970)
Southwestern corn borer	3G	FG	0.5	4	(2.0)	(3.34)	9.10	10.00	(22.44)	Henderson and Davis (1970)
Southwestern corn borer	3G	FG	0.5	4	18.0	30.06	9.10	10.00	10.96	Henderson and Davis (1970)
Southwestern corn borer	3G	FG	0.5	4	16.0	26.72	9.10	10.00	7.62	Henderson and Davis (1970)
Rootworm	10G	B	0.92	1	13.8	23.05	4.19	-	18.86	Petty and Kuhlman (1972)
Rootworm	10G	B	0.9	1	13.3	22.21	4.10	-	18.11	Kuhlman and Petty (1973)

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[a] FG = Foliar granules
B = Banded
F = Furrow

[b] Data in parentheses indicate decreases in yield, income, and economic benefit.

[c] Granules - $4.55/lb; 4 F formulation - $6.86/lb (Skoerler, 1975).

[d] Foliar application - $1.50/acre; granular applications not applied at planting = $2.50/acre.

Table 35. Summary of Carbofuran Tests on Peanuts

Pest	Formulation	Application Rate (lb/acre)	Method a/	Yield Increase b/ (lb/acre)	Additional Income b/ at 14.7¢/lb ($/acre)	Carbofuran Costs c/ ($/acre)	Application Cost d/ ($/acre)	Economic Benefit b/ ($/acre)	Source
Nematodes	10G	4.0	B	1,290	189.63	18.20	2.50	168.93	Osborne (1968)
Nematodes	10G	3.0	B	105	15.44	13.65	-	1.79	Laughlin et al. (1969)
Nematodes and thrips	10G	3.0	B	568	83.50	13.65	2.50	67.35	Minton et al. (1969)
Nematodes	10G	3.0	B	266	39.10	13.65	2.50	22.95	Morgan and Minton (1969)
Thrips	10G	3.0	B	764	112.31	13.65	2.50	96.16	Morgan and Minton (1969)
Nematodes and thrips	10G	3.0 + 2.0	B	812	119.36	22.75	2.50	94.11	Minton and Morgan (1970)
Nematodes and thrips	10G	3.0	B	131	19.26	13.65	-	5.61	Minton and Morgan (1970)
Nematodes and thrips	10G	5.0	B	62	9.10	22.75	-	(13.64)	Minton and Morgan (1970)
Nematodes and thrips	10G	3.0 + 2.0	B	232	34.10	22.75	2.50	8.85	Minton et al. (1970)
Nematodes and thrips	10G	5.0	B	147	21.61	22.75	-	(1.14)	Minton et al. (1970)
Nematodes and thrips	10G	3.0	B	114	16.76	13.65	-	3.11	Minton et al. (1970)
Nematodes and thrips	10G	5.0	B	931	136.86	22.75	-	14.11	Morgan and Minton (1970)
Nematodes and thrips	10G	3.0	B	810	119.07	13.65	-	105.42	Morgan and Minton (1970)
Nematodes and thrips	10G	3.0 + 2.0	B	692	101.72	22.75	2.50	76.47	Morgan and Minton (1970)
Nematodes	10G	5.0	B	370	54.39	22.75	2.50	29.14	Osborne (1970)
Nematodes	10G	3.0	B	300	44.10	13.65	2.50	27.95	Osborne (1970)
Nematodes	10G	2.0	B	1,028	151.12	9.10	2.50	139.52	Osborne (1970)
Nematodes	10G	2.0	B	522	76.73	9.10	2.50	65.13	Osborne (1970)
Nematodes	10G	4.0	B	362	53.21	18.20	-	35.01	Dickson et al. (1971)
Nematodes	10G	3.0	B	731	107.46	13.65	2.50	91.31	Kinloch (1971)
Nematodes and thrips	10G	5.0	B	1,337	196.54	22.75	2.50	171.29	Minton and Morgan (1971)
Nematodes, thrips, and leafhoppers	10G	5.0	B	620	91.14	22.75	2.50	65.89	Morgan and Minton (1971)
Nematodes, thrips, and leafhoppers	10G	3.0	B	(11)	(1.62)	13.65	2.50	(17.77)	Morgan and Minton (1971)
Nematodes and thrips	10G	3.0	B	392	57.62	13.65	2.50	41.47	Morgan et al. (1971)
Nematodes and thrips	10G	5.0	B	327	48.07	22.75	2.50	22.82	Morgan et al. (1971)
Nematodes and thrips	10G	5.0	B	465	68.36	22.75	2.50	43.11	Minton and Morgan (1972)
Nematodes and thrips	4F	5.0	S	443	65.12	34.30	1.50	29.32	Minton and Morgan (1972)
Nematodes	10G	4.0	FU	485	71.30	18.20	-	53.10	Sturgeon and Shackelford (1972)
Nematodes	10G	2.0	FU	423	62.18	9.10	-	53.08	Sturgeon and Shackelford (1972)
Nematodes	10G	1.0 + 2.0	FU + B	105	15.44	13.65	2.50	(0.71)	Sturgeon and Shackelford (1972)
Nematodes	10G	2.0 + 1.0	B	1,110	163.17	18.20	2.50	142.47	Sturgeon et al. (1973)
Nematodes	10G	2.0	B	261	38.37	9.10	-	27.27	Sturgeon et al. (1973)
Thrips	10G	4.0	B	(357)	(52.48)	18.20	-	(70.68)	Smith (1972)
Thrips	10G	1.0	B	(412)	(60.56)	4.55	-	(65.11)	Smith (1972)
Thrips	10G	1.0	B	(35)	(5.14)	4.55	2.50	(12.19)	Morgan et al. (1970)

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a/ S = Spray application.
FU = Furrow application.
B = Banded application.

b/ Data in parentheses indicates decreases in yield, income and economic benefit.

c/ Granules - $4.55/lb AI; 4F formulation - $6.86/lb AI (Shmerler, 1975).

d/ Spray application - $1.50/acre; granular applications not applied at planting - $2.50/acre.

Table 16. Summary of Carbofuran Tests on Potatoes.

Pest	Formulation	Method[a]	Rates (lb/acre)	Yield Increase[b] (cwt/acre)	Additional Income[b] at $2.99/cwt ($/acre)	Carbofuran Cost[c] ($/acre)	Application Cost[d] ($/acre)	Economic Benefit[b] ($/acre)	Source
Colorado potato beetle	10G	B	2.0	187	559.13	9.10	2.50	547.53	Hofmaster and Waterfield (1972)
Colorado potato beetle	10G	B	2.0	191	571.09	9.10	2.50	559.49	Hofmaster and Waterfield (1972)
Colorado potato beetle	10G	B	2.0	213	636.87	9.10	2.50	625.27	Hofmaster and Waterfield (1972)
Colorado potato beetle	10G	B	3.0	209	624.91	13.65	2.50	608.76	Hofmaster and Waterfield (1972)
Colorado potato beetle	4F	B	2.0	142	424.58	13.72	1.50	409.36	Hofmaster and Waterfield (1972)
Colorado potato beetle	4F	B	2.0	140	418.60	13.72	1.50	403.38	Hofmaster and Waterfield (1972)
Colorado potato beetle	10G	B	2.0	171	511.29	9.10	2.50	499.69	Hofmaster and Waterfield (1972)
Colorado potato beetle	10G	B	2.0	134	400.66	9.10	2.50	389.06	Hofmaster and Waterfield (1972)
Colorado potato beetle	10G	B	2.0	150	448.50	9.10	2.50	436.90	Hofmaster and Waterfield (1972)
Flea beetles	4F	S	0.5	78	233.22	3.43	1.50	228.29	Chapman (1971)
Flea beetles	4F	S	1.0	53	158.47	6.86	1.50	150.11	Chapman (1971)
Flea beetles	10G	FU	1.0	57	170.43	4.55	-	165.88	Chapman (1971)
Flea beetles	10G	FU	3.0	25	74.75	13.65	-	61.10	Chapman (1971)
Potato leafhopper	10G	B	2.0	85	254.15	9.10	-	245.05	Wells (1971)
Potato aphids	10G	B	3.0	87	260.14	13.65	-	246.48	Wells (1971)
Green peach aphid	10G	B	1.18	72	215.28	5.37	-	209.91	FMC (1971)
Colorado potato beetle	10G	B	3.0	85	254.15	13.65	-	240.50	FMC (1971)
Colorado potato beetle	10G	SD	3.0	128.4	383.92	13.65	2.50	367.77	Semel and Wilde (1969)
Colorado potato beetle	10G	FU	3.0	128.1	383.02	13.65	-	369.37	Semel and Wilde (1969)
Colorado potato beetle	10G	SD	3.0	194.6	581.85	13.65	2.50	565.70	Semel and Wilde (1969)
European corn borer	10G	B	2.0	181	541.19	9.10	-	532.09	Hofmaster and Waterfield (1969)
Green peach aphids	10G	B	2.0	174	520.26	9.10	-	511.16	Hofmaster and Waterfield (1969)
Green peach aphids	4F	S	0.5	148	442.52	3.43	1.50	437.59	Hofmaster and Waterfield (1969)

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a/ B = Banded application.
FU = Furrow application.
S = Spray application.
SD = Side-dressed.

b/ Data in parentheses indicate decreases in yield, income, and economic benefit.

c/ Granules - $4.55/lb AI 4F - $6.86/lb AI (Shmerler, 1975).

d/ Spray application - $1.50/acre; granular application, applied at planting - $2.50/acre.

Table 37. Summary of Carbofuran Tests on Rice.

Pest	Applications			Yield Increase[b] (lb/acre)	Additional Income[b] at $8.72/cwt ($/acre)	Carbofuran Cost[c] at $4.55/lb ($/acre)	Application Cost[d] ($/acre)	Economic Benefit[b] ($/acre)	Source
	Formulation	Method[a]	Rates (lb/acre)						
Rice water weevil	3G	BR	0.5	86	7.50	2.28	1.25	3.97	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	275	23.98	2.28	1.25	20.45	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	246	21.45	2.28	1.25	17.92	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	412	27.21	2.28	1.25	32.40	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	123	10.73	2.28	1.25	7.20	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	400	34.88	2.28	1.25	31.35	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	560	48.83	2.28	1.25	45.30	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	349	30.43	2.28	1.25	26.90	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	235	20.49	2.28	1.25	16.96	Gifford et al. (1975)
Rice water weevil	3G	BR	0.5	614	53.54	2.28	1.25	50.01	Gifford et al. (1975)
Rice water weevil	3G	BR	0.25	270	23.54	1.14	1.25	2.15	Gifford and Trahan (1969)
Rice water weevil	3G	BR	0.50	(199)	(17.35)	2.28	1.25	(20.88)	Gifford and Trahan (1969)
Rice water weevil	3G	BR	0.25	13	1.13	1.14	1.25	(1.26)	Gifford and Trahan (1969)
Rice water weevil	3G	BR	0.50	(16)	(1.40)	2.28	1.25	(4.93)	Gifford and Trahan (1969)
Rice water weevil	3G	BR	0.50	326	28.43	2.28	1.25	24.90	Gifford and Trahan (1969)

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a/ BR = Broadcast.
b/ Data in parentheses indicate decreases in yields, income, and economic benefit.
c/ Shmerler (1975).
d/ Broadcast applications - $1.25/acre.

Table 38. Summary of Carbofuran Tests on Sugarcane.

Pest	Applications				Yield Increase (tons/acre)	Additional Income at $12.53/ton ($/acre)	Carbofuran Costs[b] ($/acre)	Application Cost[c] ($/acre)	Economic Benefit ($/acre)	Source
	Formulation	Method[a]	Rate (lb/acre)	No.						
Soil insects	10G	B	2.85	1	15.0	187.95	12.97	2.50	172.48	Valdes, 1972a
Soil insects	10G	B	3.0	1	4.7	58.89	13.65	2.50	42.74	Broadus, 1973d
Soil insects	10G	B	3.0	1	5.0	62.65	13.65	2.50	46.50	Broadus, 1973c
Soil insects	10G	B	3.0	1	2.9	36.34	13.65	2.50	20.19	Broadus, 1973e
Soil insects	10G	B	3.14	1	14.7	184.19	14.29	2.50	167.40	Valdes, 1972a
Soil insects	10G	B	3.63	1	4.58	57.39	16.52	2.50	38.37	Valdes, 1972b

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a/ B = Banded application.
b/ Granules - $4.55/lb AI (Shmerler, 1975).
c/ Banded applications - $2.50/acre.

Table 39. Summary of Carbofuran Tests on Tobacco.

Pest	Applications				Yield Increase (cured lb/acre)	Additional Income at $.839/lb ($/acre)	Carbofuran Costs b/ ($/acre)	Application Cost c/ ($/acre)	Economic Benefit ($/acre)	Source
	Formulation	Methods a/	Rate (lb/acre)	No.						
Root-knot nematode	10G	B	6.0	1	578	484.94	27.30	2.50	455.14	Nance, 1972
Root-knot nematode	10G	B	6.0	1	304	255.06	27.30	2.50	225.26	Metz, 1973c
Root-knot nematode	10G	B	6.0	1	278	233.24	27.30	2.50	203.44	Nance, 1972
Root-knot nematode	10G	B	6.0	1	138	115.78	27.30	2.50	85.98	Nance, 1972
Root-knot nematode	10G	B	6.0	1	102	85.58	27.30	2.50	55.78	Nance, 1972
Tobacco flea beetle, tobacco thrip, and green peach aphid	10G	B	4.0	1	456	382.58	18.20	2.50	366.88	Moore, 1971
Not identified	10G	B	5.0	1	161	135.08	22.75	2.50	109.83	Pless et al., 1971
Not identified	10G	B	5.0	1	152	127.53	22.75	2.50	102.28	Pless et al., 1971

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a/ B = Banded application.

b/ Granules - $4.55/lb AI (Schmerler, 1975).

c/ Banded applications - $2.50/acre.

Table 40. Summary of Carbofuran Tests on Peppers.

Pest	Applications			Yield increase (cwt/acre)	Additional income at $12.97/cwt ($/acre)	Carbofuran costs at $4.55/lb b/ ($/acre)	Application cost c/ ($/acre)	Economic benefit ($/acre)	Source
	Formulation	Methods a/	Rates (lb/acre)						
European corn borer	10G	SD	3.0	58	752.26	13.65	2.50	736.11	Ryder etal.(1969)
European corn borer	10G	SD	2.0 + 3.0	72	933.84	22.75	5.00	906.09	Burbutis & Lesiewicz (1974)
European corn borer	10G	SD	2.0 + 3.0	82	1,063.54	22.75	5.00	1,035.79	Burbutis & Kelsey (1971)
European corn borer	10G	SD	2.0 + 3.0	32	415.04	18.20	5.00	391.84	Burbutis & Kelsey (1972)
European corn borer	10G	SD	3.0	22	285.34	13.65	2.50	269.19	Burbutis & Kelsey (1971)
European corn borer	10G	SD	4.0	78	1,011.66	18.20	2.50	990.96	Burbutis & Kelsey (1971)
European corn borer	10G	SD	2.0 + 2.0	55.7	722.43	18.20	5.00	699.23	Hofmaster (1971)
European corn borer	10G	SD	2.0 + 3.0	54.8	710.76	22.75	5.00	683.01	Hofmaster (1971)

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a/ SD = Side-dressed.

b/ Shmerler (1975).

c/ Side-dressed applications - $2.50/acre/application

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